

(19)



Eur päisches Patentamt

Eur pean Pat nt Offic

Office européen des brevets



(11) Publication number:

0 516 069 A1

(12)

EUROPEAN PATENT APPLICATION(21) Application number: **92108916.5**(22) Date of filing: **27.05.92**

(51) Int. Cl.⁵: **C07D 213/81, C07D 277/46, C07D 401/06, C07D 401/12, C07D 401/14, C07D 417/12, C07D 417/14, C07D 241/24, C07C 233/82, A61K 31/44, A61K 31/425**

(30) Priority: **31.05.91 JP 157725/91**

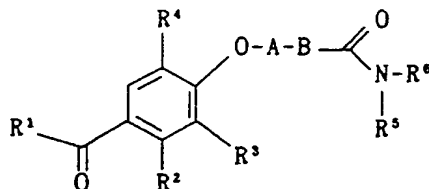
(43) Date of publication of application:
02.12.92 Bulletin 92/49

(84) Designated Contracting States:
AT BE CH DE DK ES FR GB GR IT LI NL PT SE

(71) Applicant: **SUMITOMO PHARMACEUTICALS COMPANY, LIMITED**
2-8, Doshomachi 2-chome, Chuo-ku
Osaka-shi Osaka 541(JP)

(72) Inventor: **Nagata, Hideo**
2-29-7, Ooike
Ibaraki-shi, Osaka 567(JP)
Inventor: **Kawakami, Hajime**
6-32-702, Fukazu-cho
Nishinomiya-shi, Hyogo 663(JP)

(74) Representative: **von Kreisler, Alek,**
Dipl.-Chem. et al
Patentanwälte Von Kreisler-Selting-Werner,
Delchmannhaus am Hauptbahnhof
W-5000 Köln 1(DE)

(54) **Leukotriene B₄ antagonist.**(57) **Leukotriene B₄ antagonists of the formula:**

wherein each symbol is as defined in the specification, processes for producing them, and pharmaceutical compositions containing them. The compounds of the present invention are very useful as the drugs for the treatment of allergic and inflammatory diseases.

EP 0 516 069 A1

BACKGROUND OF THE INVENTION

TECHNICAL FIELD

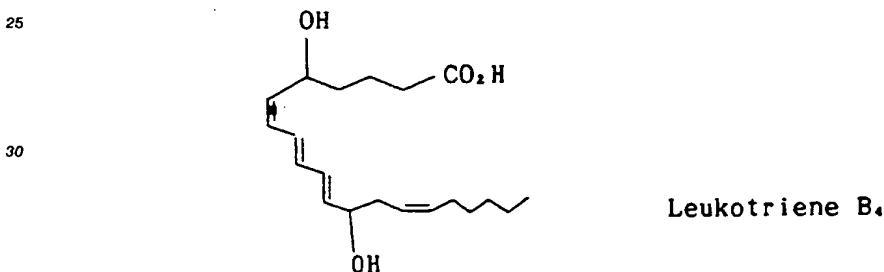
5 The present invention relates to compounds effective as leukotriene B₄ antagonists.
 More particularly, this invention relates to leukotriene B₄ antagonists, to processes for producing them and to pharmaceutical compositions containing at least one of those leukotriene B₄ antagonists, which have excellent anti-leukotriene B₄ activity and are useful as an anti-allergic agent or an anti-inflammatory agent.

PRIOR ART

10 In 1979 B. Samuelsson reported the isolation and biological effects of leukotrienes (B. Samuelsson et al. (1980): Advances in Prostaglandin and Thromboxane Research, Vol. 6, edited by B. Samuelsson, R. Ramwell, and R. Paoletti, P. I. Raven Press, New York).

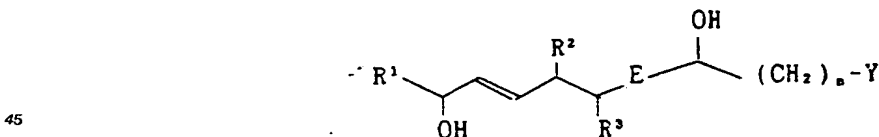
15 Since then, a tremendous amount of research in the synthetic organic chemistry and pharmacology of leukotriene A₄, B₄, C₄, D₄, etc. has been performed.

Leukotrienes induce an increase in capillary permeability and cause smooth muscle contraction. Leukotriene B₄, one of leukotrienes which is shown below, has different pharmacological properties from the others. It is chemotactic for macrophages and neutrophils at concentrations of ~ 1 ng/ml (greater than any
 20 other known lipid chemotactic factor). It is detected in the synovia of patients with rheumatoid arthritis or gouty arthritis, and in the sputum of obstructive airways diseases which suggest that it is a primary mediator of inflammatory and allergic states.



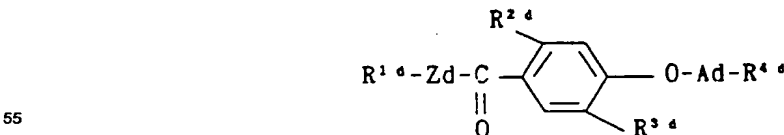
In recent research some compounds having an antagonism on LTB₄ have been reported. For example,
 1) EP-A-0183177 (SUMITOMO PHARMACEUTICALS CO.)

40

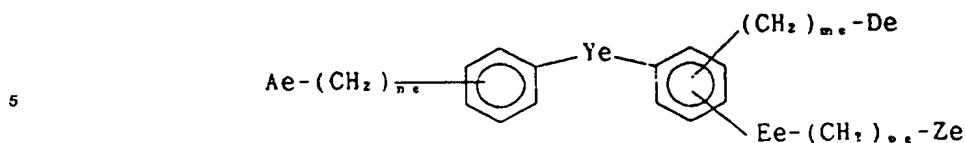


2) EP-A-276065 (ELI LILLY & CO)

50



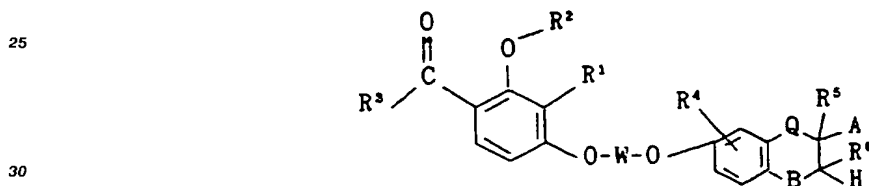
3) EP-A-276064 (ELI LILLY & CO)



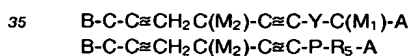
4) EP-A-0405116 (ONO PHARMACEUTICAL CO)



5) EP-A-292977 (SEARLE G D & CO)



6) WO-A-8805045 (UPJOHN CO)



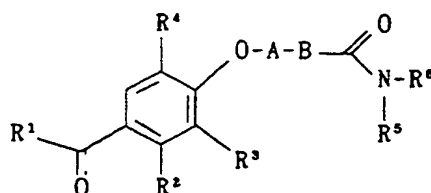
SUMMARY OF THE INVENTION

40 In accordance with the present invention, leukotriene B₄ antagonists of the following general formula [I] and their non-toxic pharmaceutically acceptable salts are provided, which have potent anti-leukotriene B₄ activity which include suppression of chemotaxis, degranulation and O₂-production of leukocytes, and modulation of lymphocytes activity, etc. This action may render these compounds very useful as the drugs for the treatment of inflammatory states or immunological disorders such as allergy, rheumatoid arthritis, inflammatory bowel disease.

DISCLOSURE OF THE INVENTION

50 The novel leukotriene B₄ antagonists provided by the present invention are those represented by the formula [I]:

55



5

10

wherein

A is a C₁-C₅ alkylene chain;

B is a phenylene or 6 membered heteroaromatic group which is constituted by carbon atoms and one or two nitrogen atoms, and B may be, optionally substituted with one or two substituents selected from the group, consisting of a C₁-C₅ alkyl group, a C₁-C₅ alkoxy group, a hydroxyl group, a carboxyl group, a nitro group and a halogen atom;

15

R¹ is a C₁-C₅ alkyl group;

R² is a hydroxyl group or a C₁-C₅ alkoxy group;

20

R³ and R⁴ are each independently a hydrogen atom, a C₁-C₅ alkyl group, a C₂-C₅ alkenyl group or a C₂-C₅ alkynyl group;

R⁵ is a hydrogen atom, a C₁-C₅ alkyl group or a hydroxy C₁-C₅ alkyl group;

R⁶ is a group of the formula:

-X-Y-Z-R^{6'}

25

wherein X is a phenylene group or a monocyclic 5- 6 membered hetero aromatic group, and X is optionally substituted with one or two substituents selected from the group consisting of a C₁ -C₅ alkyl group, a hydroxyl group, a carboxyl group, a nitro group and a halogen atom;

Y is a single bond or an oxygen atom;

30

Z is a single bond or a C₁-C₅ alkylene chain;

provided that when Y is an oxygen atom,

X is a phenylene group and Z is a C₁-C₅ alkylene chain;

R^{6'} is a COOR⁷ group,

a CONR⁸R⁹ group,

35

a CONHCHR²⁰(CH₂)_nCOOR⁷ group,

a CONHCHR²⁰(CH₂)_nCONR⁸R⁹ group,

a CONHCHR²⁰CONHCHR²²CO₂R⁷ group or

a sulfamoyl group,

wherein R⁷ is a hydrogen atom, a benzyl group, a C₁-C₅ alkyl group or an C₁-C₅ alkyl group

40

substituted with an aminoheteroaromatic group wherein the heteroaromatic group is a monocyclic 5-6 membered heteroaromatic group;

R⁸ and R⁹ are each independently a hydrogen atom, a C₁-C₅ alkyl group, hydroxy C₁ -C₅ alkyl group, a hydroxyethylpyridyl group or a hydroxyethylthiazolyl group, or the group of the formula:

45

-NR⁸R⁹

represents a pyrrolidino, a piperidino or a morpholino group;

R²⁰ is a hydrogen atom, a hydroxyl group, a C₁-C₅ alkyl group, a phenyl group, a hydroxyphenyl group, a benzyl group, a hydroxy benzyl group or a substituted C₁-C₅ alkyl group wherein the substituent is selected from the group consisting of a hydroxyl group, a C₁-C₅ alkoxy group, a mercapto group, a methylthio group, an amino group, an indolyl group, an imidazolyl group, a carboxyl group, a C₁-C₅ alkoxy carbonyl group, a carbamoyl group and a guanidino group;

50

n is 0, 1, 2, 3, 4 or 5; and

R²² is a hydrogen atom, a C₁-C₅ alkyl group or a C₁-C₅ hydroxyalkyl group;

55

or R⁶ is a CHR²⁰(CH₂)_nCOOR⁷ group,

a CH₂CHR²⁰COOR⁷ group,

a CHR²⁰(CH₂)_nCONR⁸R⁹ group,

a CH₂CHR²⁰CONR⁸R⁹ group,

- a $\text{CHR}^{20}(\text{CH}_2)_n\text{OH}$ group,
 a $\text{CR}^{20}\text{R}^{22}(\text{CH}_2)_n\text{OH}$ group,
 a $\text{CH}_2\text{CHR}^{20}\text{OH}$ group, or
 a $\text{CHR}^{20}\text{CONHCHR}^{22}\text{CO}_2\text{R}^7$ group,
 5 wherein R^7 , R^8 , R^9 , R^{20} , R^{22} and n are as defined above, or the group of the formula:



10

represents an azetidino group, pyrrolidino group, a piperidino group or a homopiperidino group, which is optionally substituted with one to two substituents selected from the group consisting of a hydroxyl group, a $\text{C}_1\text{-C}_5$ hydroxyalkyl group, carboxyl group, $\text{C}_1\text{-C}_5$ alkoxycarbonyl group and benzyloxycarbonyl group; or
 15 pharmaceutically acceptable salts thereof.

In the definitions as used above, the term " $\text{C}_1\text{-C}_5$ alkylene" means a straight or branched chain $\text{C}_1\text{-C}_5$ alkylene (e.g. methylene, ethylene, trimethylene, tetramethylene, pentamethylene, 1-methylethylene, 2-ethyltrimethylene, etc.).

20 The term " $\text{C}_1\text{-C}_5$ alkyl" means a straight or branched chain $\text{C}_1\text{-C}_5$ alkyl (e.g. methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, n-pentyl, iso-pentyl, sec-pentyl, neo-pentyl, etc.).

The term " $\text{C}_2\text{-C}_5$ alkenyl" means a straight or branched chain $\text{C}_2\text{-C}_5$ alkenyl (e.g. 1-methylethenyl, 1-ethylethenyl, 1-propenyl, 2-propenyl, 1-methyl-1-propenyl, 2-methyl-1-propenyl, 1-methyl-2-propenyl, 2-methyl-2-propenyl, 1,2-dimethyl-1-propenyl, 1-n-butenyl, 2-n-butenyl, 3-n-butenyl, 1-methyl-1-butenyl, 2-methyl-1-butenyl, 3-methyl-1-butenyl, 1-methyl-2-butenyl, 2-methyl-3-butenyl, 3-methyl-3-butenyl, 1-pentenyl, 2-pentenyl, 3-pentenyl, 4-pentenyl, etc.).

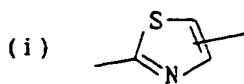
The term " $\text{C}_2\text{-C}_5$ alkynyl" means a straight or branched chain $\text{C}_2\text{-C}_5$ alkynyl (e.g. ethynyl, 1-propynyl, 2-propynyl, 1-methyl-2-propynyl, 1-n-butylnyl, 2-n-butylnyl, 3-n-butylnyl, 3-methyl-1-butylnyl, 1-methyl-2-butylnyl, 2-methyl-3-butylnyl, 1-pentylnyl 2-pentylnyl 3-pentylnyl, 4-pentylnyl, etc.).

30 The term " $\text{C}_1\text{-C}_5$ alkoxy" means alkoxy having $\text{C}_1\text{-C}_5$ alkyl moiety (e.g. methoxy, ethoxy, n-propoxy, iso-propoxy, n-butoxy, iso-butoxy, sec-butoxy, tert-butoxy, n-pentoxy, iso-pentoxy, sec-pentoxy, neo-pentoxy, etc.).

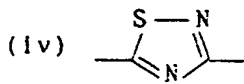
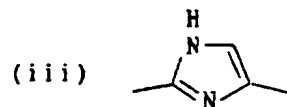
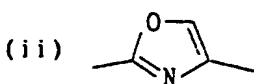
The term "6 membered heteroaromatic group which is constituted by carbon atoms and one or two nitrogen atoms" includes pyridinediyl, pyrazinediyl, pyrimidinediyl, etc.

35 The term "monocyclic 5-6 membered heteroaromatic group" contains, for example, 1-3 hetero atoms which can be a nitrogen, oxygen or sulfur atom, or an oxydized nitrogen atom ($\text{N} \rightarrow \text{O}$), and examples of the monocyclic 5-6 membered heteroaromatic group are a pyridinediyl group and any one of the group of the formula (i)-(viii):

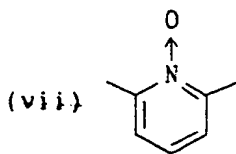
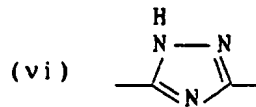
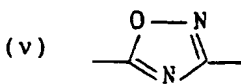
40



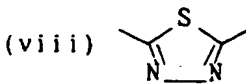
45



50



55



The term "hydroxyphenyl group" may be a 2-hydroxyphenyl, a 3-hydroxyphenyl or a 4-hydroxyphenyl group.

The term "hydroxybenzyl group" may be a 2-hydroxybenzyl, a 3-hydroxybenzyl or a 4-hydroxybenzyl group.

5 The term "halogen" may be a chlorine, a bromine or a fluorine atom.

The term "indolyl group" may be a 2-indolyl or 3-indolyl group.

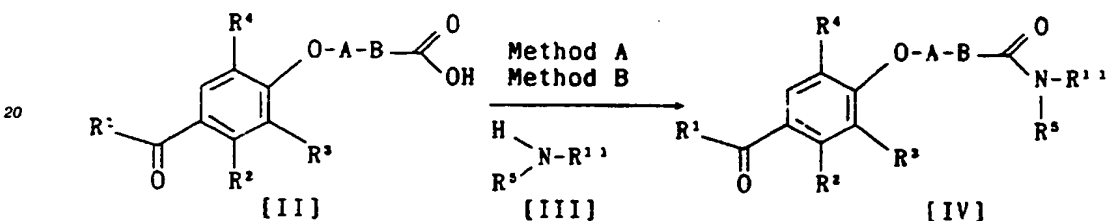
The term "imidazolyl group" may be a 4-imidazolyl group.

A basic object of the present invention is to provide novel compounds effective as leukotriene B₄ antagonists [I] having excellent pharmacological activities.

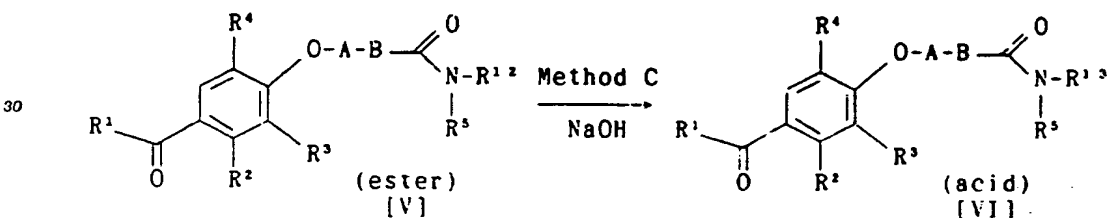
10 Another object of the present invention is to provide processes for producing those compounds [I]. A further object of the present invention is to provide a pharmaceutical composition containing a compound of the formula [I]. These and other objects will be apparent to those skilled in the art to which the present invention pertains from the foregoing and subsequent descriptions.

The novel leukotriene B₄ antagonists [I] of the invention can be prepared by the following methods:

15



25



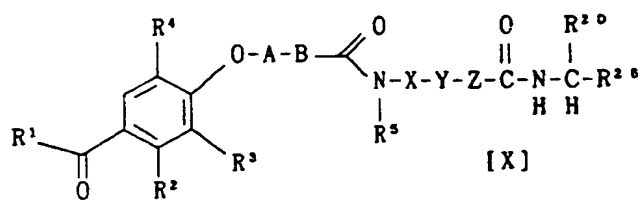
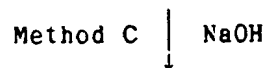
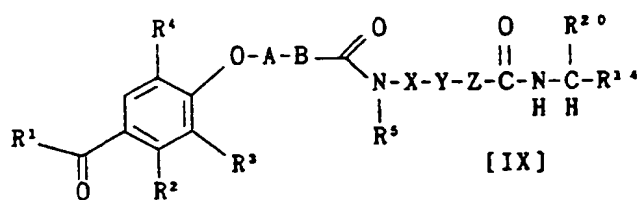
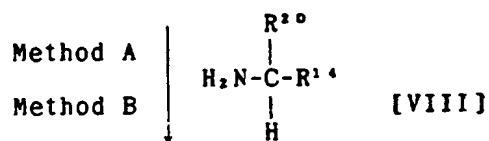
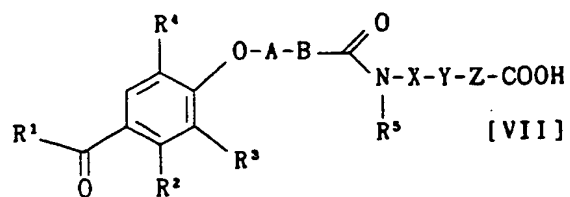
35

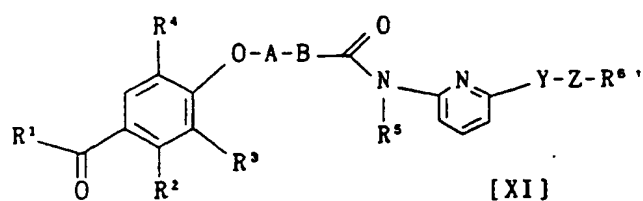
40

45

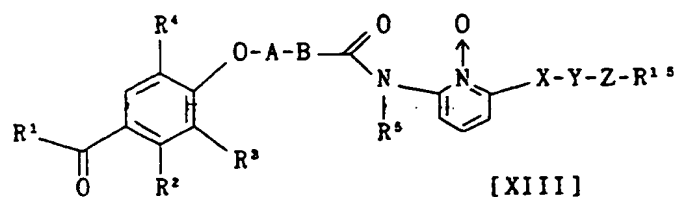
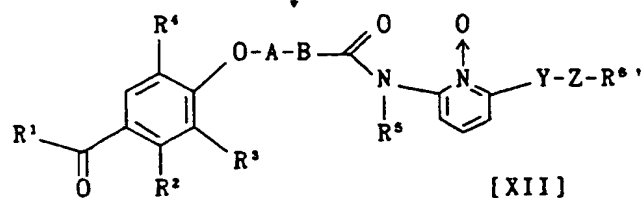
50

55

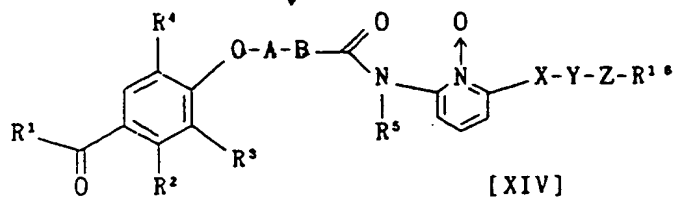




Method D ↓



Method C ↓



35

(wherein A, B, R¹, R², R³, R⁴, R⁵, R⁶, X, Y, Z and R²⁰ are as defined above, and
R¹¹ is the same as R⁶, but it does not mean free carboxylic group;
R¹² is a group of the formula:

- 40
- 50 X-Y-Z-COOR⁷,
X-Y-Z-CONHCHR²⁰(CH₂)_nCOOR⁷,
X-Y-Z-CONHCHR²⁰CONHCHR²²CO₂R⁷,
CHR²⁰(CH₂)_nCOOR⁷,
CH₂CHR²⁰COOR⁷, or
55 CHR²⁰CONHCHR²²COOR⁷,

wherein X, Y, Z, R²⁰, R²² and n are as defined above, and R⁷ is the same as R⁷ but it does not mean a hydrogen atom,

R¹³ is a group of the formula:

X-Y-Z-COOH,
 X-Y-Z-CONHCHR²⁰(CH₂)_nCOOH,
 5 X-Y-Z-CONHCHR²⁰CONHCHR²²CO₂H,
 CHR²⁰(CH₂)_nCOOH,
 CH₂CHR²⁰COOH, or
 CHR²⁰CONHCHR²²COOH,

10 wherein X, Y, Z, R²⁰, R²² and n are as defined above.

R¹⁴ is a group of the formula:

(CH₂)_nCOOR^{7'}, or
 CONHCHR²²COOR^{7'},

15 wherein R^{7'}, R²² and n are as defined above.

R¹⁵ is a group of the formula:

COOR^{7'},
 20 CONHCHR²⁰(CH₂)_nCOOR^{7'}, or
 CONHCHR²⁰CONHCHR²²CO₂R^{7'},

wherein R^{7'}, R²⁰, R²² and n are as defined above.

R¹⁶ is a group of the formula:

25 COOH,
 CONHCHR²⁰(CH₂)_nCOOH, or
 CONHCHR²⁰CONHCHR²²CO₂H,

30 wherein R²⁰, R²² and n are as defined above.

R²⁶ is a group of the formula:

(CH₂)_nCOOH, or
 CONHCHR²²COOH,

35 wherein R²² and n are as defined above.

Method A

40 The amide compound [IV] or [IX] can be prepared from an acid compound [II] or [VII] by reacting an amine compound [III] or [VIII] in the presence of a condensing agent (e.g. dicyclohexylcarbodiimide, ethyldimethylaminopropylcarbodiimide hydrochloride, etc.), hydroxybenzotriazole and a tertiary amine (e.g. triethylamine, 4-dimethylaminopyridine, etc.) in an inert solvent (e.g. dichloromethane, mixed solvent of dichloromethane and N,N-dimethylformamide, etc.) at a temperature in the range from 0 °C to the boiling

45 temperature of the solvent.

If a substituent of R²⁰ of compound [VIII] is an impediment group (e.g. mercapto, carboxyl, amino group, etc.), the compound is previously protected by a protecting group (e.g. benzyl, benzyloxycarbonyl, t-butoxycarbonyl group, etc.), and after the reaction is carried out, the protecting group is eliminated. The protection and deprotection of R²⁰ can be carried out by the conventional procedure. [Protective Group in

50 Organic Chemistry, Edited by J. F. W. McOmic (1973) 95 - 143].

Method B

55 The amide compound [IV] or [IX] can be obtained from an acid chloride or an acid anhydride of an acid compound [II] or [VII] by reacting with an amine compound [III] or [VIII] in the presence of a tertiary amine (e.g. triethylamine, etc.), or by reacting with a salt of an amine compound [III] or [VIII] (e.g. sodium salt, potassium salt, etc.) in the absence of amine in an inert solvent (e.g. tetrahydrofuran, etc.) at a temperature in the range from 0 °C to a boiling temperature of the solvent.

The transformation of an acid group to an acid chloride group can be carried out by treating the acid compound with phosphorous oxychloride or thionyl chloride in an inert solvent (e.g. chloroform, etc.) or in the absence of solvent at a temperature in the range of from -40 °C to the boiling temperature of the reaction mixture.

5 The transformation of an acid group to an acid anhydride group can be carried out by treating the acid compound with chloroformate ester (e.g. ethyl chloroformate, etc.) in the presence of a tertiary amine (e.g. triethylamine, etc.) in an inert solvent (e.g. chloroform, etc.) at a temperature in the range of from -40 °C to the boiling temperature of the solvent.

10 If a substituent of R²⁰ of compound [VIII] is a impediment group (e.g. mercapto, carboxyl, amino group, etc.), the compound is previously protected by a protecting group (e.g. benzyl group, benzyloxycarbonyl group, t-butoxycarbonyl group, etc.), and after the reaction is carried out, the protecting group is eliminated.

The protection and deprotection of R²⁰ can be carried out by the conventional procedure [Protective Group in Organic Chemistry, Edited by J. F. W. McOmic (1973) 95 - 143].

15 Method C

The acid compound [VI], [X] or [XIV] can be prepared by hydrolysis of the ester compound [V], [IX] or [XIII] by treating with an aqueous alkali (e.g. sodium hydroxide, lithium hydroxide) in an inert solvent (e.g. tetrahydrofuran, methanol, ethanol, etc.).

20

Method D

The N-oxide compound [XII] can be prepared from pyridine compound [XI] by treating with an oxidizing agent (e.g. m-chloroperbenzoic acid, etc.) in an inert solvent (e.g. methylene chloride, etc.).

25 The amine compounds [III] and [VIII] are known compounds or easily obtained as described in e.g. J. Goto, K. Sakane, Y. Nakai, T. Teraji, The journal of antibiotics, 37, 532 (1984), I. Csendes, B. W. Müller, W. Tosch, The journal of antibiotics, 36, 1020 (1983), M. Ohta, Yakugaku zasshi, 72, 1536 (1983), JP-A-58-23697. And, the starting compounds [II], [II-1] and [II-2] can be obtained by the following method.

30

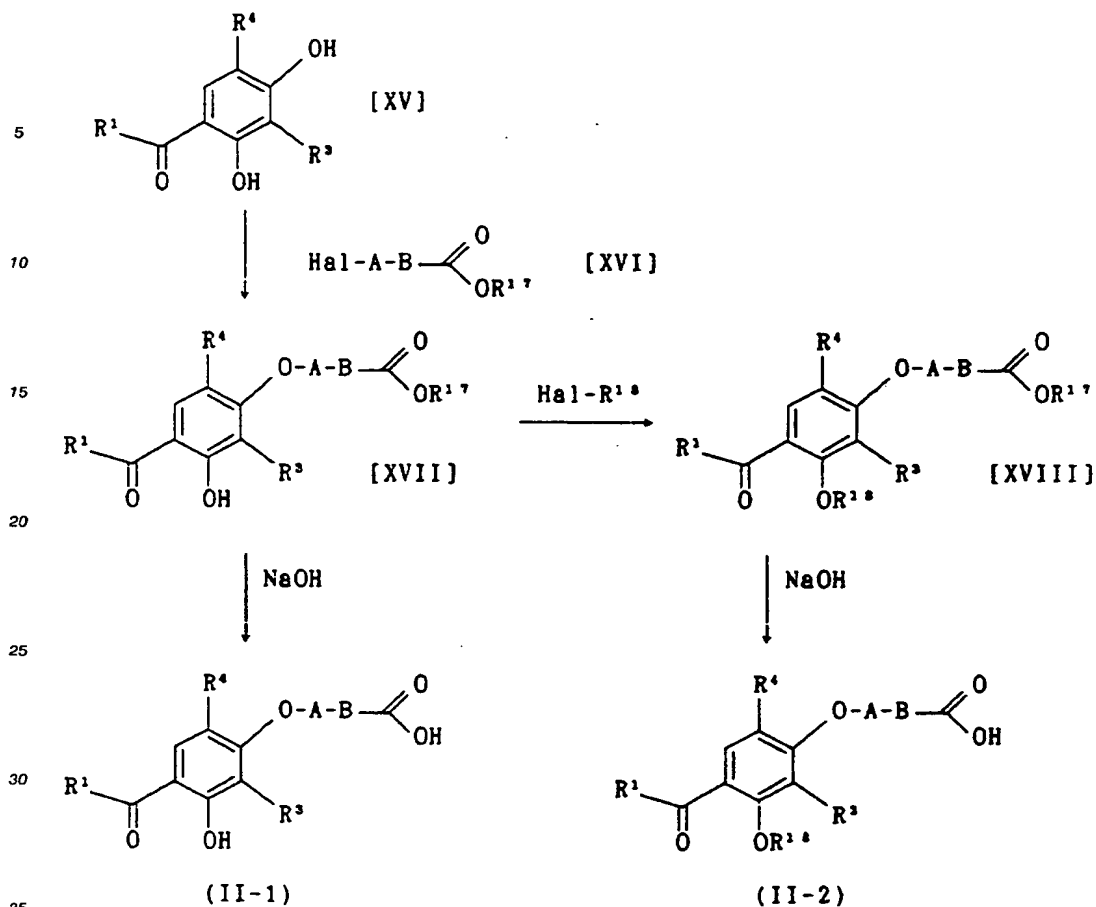
35

40

45

50

55



(wherein A, B, R¹, R², R³ and R⁴ are as defined above, R¹⁷ is a C₁-C₅ alkyl group, R¹⁸ is a C₁-C₅ alkyl group, Hal is a chlorine or bromine atom)

Alkylation of the compound [XV] into the compound [XVII] can be accomplished by treating the former with the compound [XVI] in an inert solvent (e.g. N,N-dimethylformamide, etc.) in the presence of a base (e.g. anhydrous potassium carbonate, etc.). Optionally, the compound [XVII] can be alkylated to produce the compound [XVIII] by the same procedure as used in the synthesis of the compound [XVII] from the compound [XV]. And, the compound (II-1) and (II-2), respectively, can be prepared from the compound [XVII] and [XVIII] by hydrolysis (Method C).

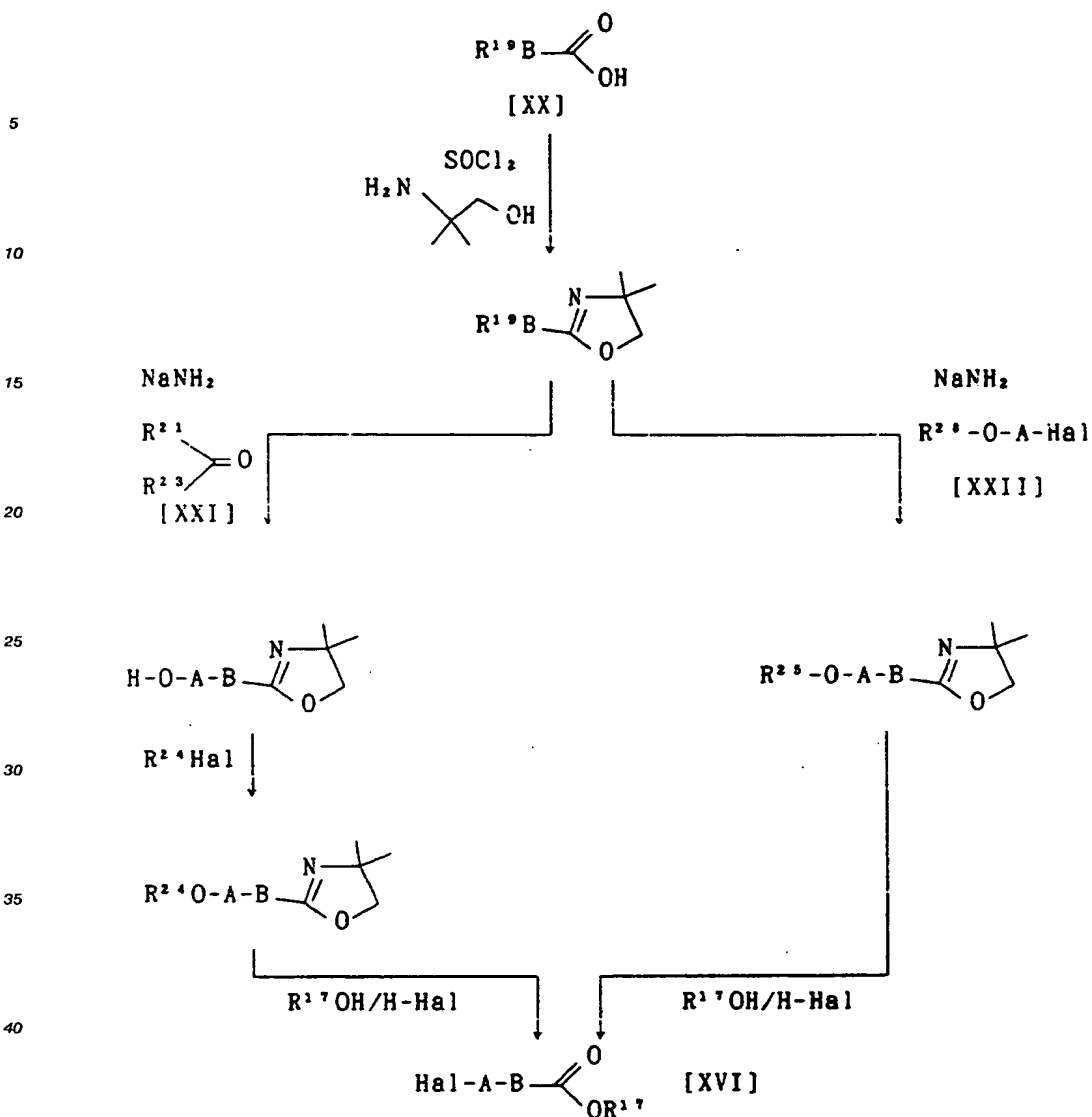
The compound [XV] is a known compound or easily obtained as described in e.g. J. Hurst, J. Wibberley, Journal of Chemical Society, 1962, 119.

The compound [XVI] is obtained by;

(1) In the case where both Hal and B of compound [XVI] are jointed to the same carbon atom:

the compound [XVI] is a known compound or easily obtained as described in e.g. J. Hurst, J. Wibberley, Journal of Chemical Society, 1962, 119, etc,

(2) In the case that there are two carbon atoms between Hal and B in compound [XVI]:



(wherein A, B and Hal are as defined above, R^{19} is a C_1-C_5 alkyl group (but, there is at least one hydrogen atom at the α carbon bonded to B), R^{21} , R^{23} are each independently a hydrogen atom or a C_1-C_5 alkyl group, R^{24} is a C_1-C_5 alkyl group, and R^{25} is a C_1-C_5 alkyl group or phenyl group)

the compound [XVI] is prepared in the following way:

first step: the carboxylic acid group of a compound [XX] is protected to yield a 4,4-dimethyl-2-oxazoline compound,

second step: the 4,4-dimethyl-2-oxazoline compound is treated with a base to deprotonate a hydrogen atom attached to a carbon atom adjacent to B group (e.g. sodium amide, n-butyl lithium, etc.),

third step: the deprotected compound is reacted with the compound of the formula [XXI] (aldehyde or ketone) to yield a hydroxy compound,

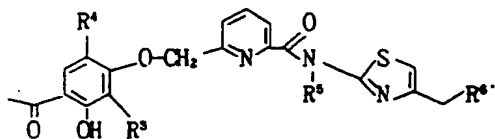
fourth step: the hydroxyl compound is alkylated by reacting with a compound of the formula $R^{24}-Hal$,

fifth step: the alkylated compound is treated with halogenated hydrogen (e.g. hydrogen chloride, hydrogen bromide, etc.) in the alcohol represented by $R^{17}OH$.

(3) In the case that there are 3 or more carbon atoms between Hal and B in the compound [XVI]:
the compound [XVI] is prepared in the same way, except modifying the alkylation reaction, as described
in above (2), i.e., the compound [XX] is protected and deprotonated, and then alkylated by alkylhalide
[XXII]. The alkylated product is treated with halogenated hydrogen (e.g. hydrogen chloride, hydrogen
bromide, etc.) in the alcohol represented by R¹⁷OH.

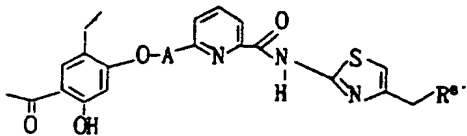
Specific examples of the leukotriene B₄ antagonists are as follows:

Table 1



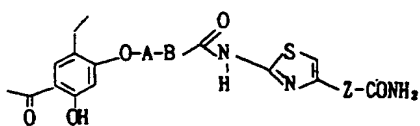
R ³	H	H	H	n-Pr	H	H	H	H	H
R ⁴	Me	n-Pr	n-Pr	H	Et	Et	Et	Et	Et
R ⁵	H	H	H	H	CH ₃	Et	n-Pr	i-Pr	H
R ⁶	CONH ₂	CONH ₂	CONH ₂	CONH ₂	CONH ₂	CONH ₂	CONH ₂	CONH ₂	CONHMe

Table 2



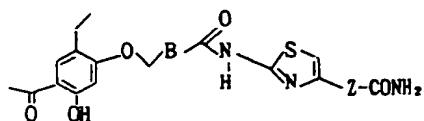
A	-CH ₂ -	-CH ₂ -	-CH ₂ -	-CH ₂ -	-CH ₂ -	-(CH ₂) ₂ -	-(CH ₂) ₃ -	-(CH ₂) ₄ -	-(CH ₂) ₅ -
R ⁶	CONMe ₂	CONHiPr				CONH ₂	CONH ₂	CONH ₂	CONH ₂

Table 3



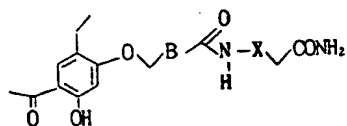
A	-CHMe-	-CH ₂ -	-CH ₂ -	-CH ₂ -	-CH ₂ -	-CH ₂ -	-CH ₂ -	-CH ₂ -	-CH ₂ -
B									
Z	-CH ₂ -	single bond	-CH ₂ -	-(CH ₂) ₂ -	-(CH ₂) ₃ -	-(CH ₂) ₄ -	-(CH ₂) ₅ -	-CH ₂ -	single bond

Table 4



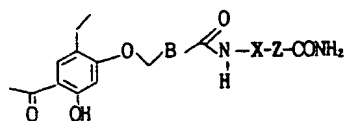
B									
Z	-CH ₂ -	-(CH ₂) ₂ -	-(CH ₂) ₃ -	-(CH ₂) ₄ -	single bond	-CH ₂ -	-(CH ₂) ₂ -	-(CH ₂) ₃ -	-(CH ₂) ₄ -

Table 5



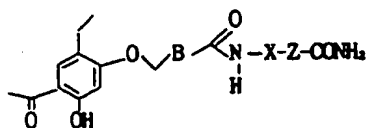
B									
X									

Table 6



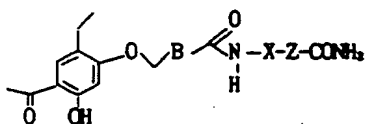
B									
X									
Z	single bond	-CH ₂ -	-(CH ₂) ₂ -	-(CH ₂) ₃ -	-(CH ₂) ₄ -	single bond	-CH ₂ -	-(CH ₂) ₂ -	single bond

Table 7



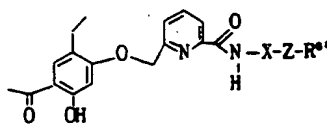
B									
X									
Z	-CH ₂ -	-(CH ₂) ₂ -	-(CH ₂) ₃ -	-(CH ₂) ₄ -	single bond	-CH ₂ -	-(CH ₂) ₂ -	single bond	-CH ₂ -

Table 8



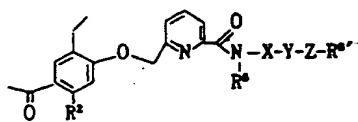
B									
X									
Z	-(CH ₂) ₂ -	-(CH ₂) ₃ -	-(CH ₂) ₄ -	-CH ₂ -	single bond	-(CH ₂) ₂ -	-(CH ₂) ₃ -	-(CH ₂) ₄ -	-CMe ₂ -

Table 9



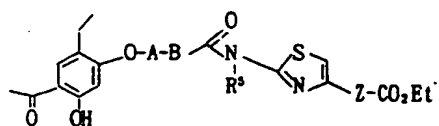
X									
Z	single bond	single bond	single bond	single bond	-CH ₂ -	-(CH ₂) ₂ -	-CH ₂ -	-(CH ₂) ₂ -	-CH ₂ -
R ⁶	CONH ₂	CONH ₂	SO ₂ NH ₂	SO ₂ NH ₂	CONH ₂	CONH ₂	SO ₂ NH ₂	SO ₂ NH ₂	SO ₂ NH ₂

Table 10



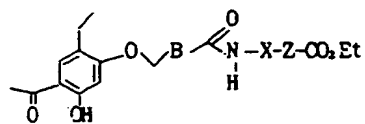
R ²	OH	OH	OH	OH	OMe	OH	OH	OH	OH
R ⁵	H	H	H	H	H	H	Me	Et	n-Pr
X									
Y	-O-	-O-	-O-	-O-	single bond	single bond	single bond	single bond	single bond
Z	-CH ₂ -	-(CH ₂) ₂ -	-CH ₂ -	-(CH ₂) ₂ -	-CH ₂ -	-CH ₂ -	-CH ₂ -	-CH ₂ -	-CH ₂ -
R ⁶	CONH ₂	CONH ₂	CONH ₂	CONH ₂	CONH ₂	CO ₂ Et	CO ₂ Et	CO ₂ Et	CO ₂ Et

Table 11



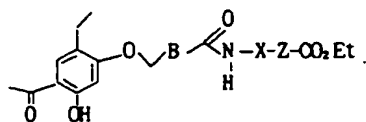
A	-CH ₂ -	-(CH ₂) ₂ -	-(CH ₂) ₃ -	-(CH ₂) ₄ -	-(CH ₂) ₅ -	-CHMe-	-CH ₂ -	-CH ₂ -	-CH ₂ -
B									
R ⁵	i-Pr	H	H	H	H	H	H	H	H
Z	-CH ₂ -	-CH ₂ -	-CH ₂ -	-CH ₂ -	-CH ₂ -	-CH ₂ -	-CH ₂ -	-(CH ₂) ₂ -	-(CH ₂) ₃ -

Table 12



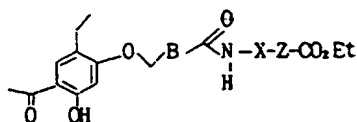
B									
X									
Z	-CH ₂ -	-(CH ₂) ₂ -	-(CH ₂) ₃ -	-CH ₂ -	-(CH ₂) ₂ -	-(CH ₂) ₃ -	-CH ₂ -	-CH ₂ -	-CH ₂ -

Table 13



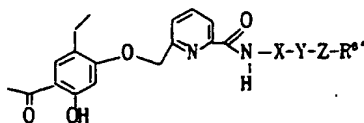
B									
X									
Z	-CH2-	-CH2-	-CH2-	-(CH2)2-	-(CH2)3-	-CH2-	-(CH2)2-	-(CH2)3-	-CH2-

Table 14



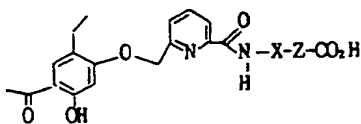
B									
X									
Z	-(CH2)2-	-(CH2)3-	-CH2-	-(CH2)2-	-(CH2)3-	-CH2-	-CH2-	-(CH2)2-	-(CH2)2-

Table 15



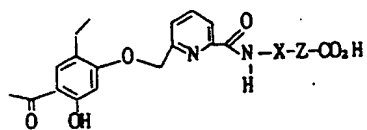
X									
Y	-O-	-O-	-O-	-O-	single bond	single bond	single bond	single bond	single bond
Z	-CH ₂ -	-CH ₂ -	-(CH ₂) ₂ -	-(CH ₂) ₂ -	single bond	-CH ₂ -	-(CH ₂) ₂ -	-(CH ₂) ₃ -	-(CH ₂) ₄ -
R ⁶	CO ₂ Et	CO ₂ Et	CO ₂ Et	CO ₂ Et	CO ₂ H	CO ₂ H	CO ₂ H	CO ₂ H	CO ₂ H

Table 16



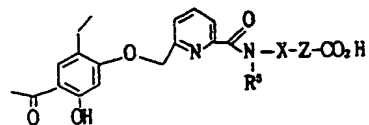
X									
Z	-(CH ₂) ₅ -	-CH ₂ -	-(CH ₂) ₂ -	-CH ₂ -	-(CH ₂) ₂ -	-CH ₂ -	-(CH ₂) ₂ -	-CH ₂ -	-(CH ₂) ₂ -

Table 17



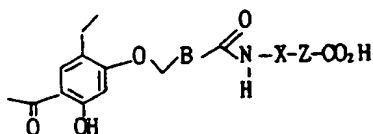
X									
Z	-CH ₂ -	-(CH ₂) ₂ -	single bond	-CH ₂ -	-(CH ₂) ₂ -	-(CH ₂) ₃ -	-(CH ₂) ₄ -	-(CH ₂) ₅ -	single bond

Table 18



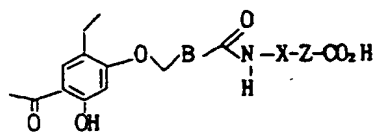
R ⁵	H	H	H	Me	Et	n-Pr	i-Pr	n-Bu	i-Bu
X									
Z	-CH ₂ -	-(CH ₂) ₂ -	-(CH ₂) ₃ -	-CH ₂ -	-CH ₂ -	-CH ₂ -	-CH ₂ -	-CH ₂ -	-CH ₂ -

Table 19



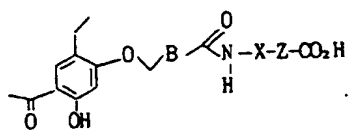
B									
X									
Z	-CH ₂ -	-(CH ₂) ₂ -	-CH ₂ -	-(CH ₂) ₂ -	-CH ₂ -	-(CH ₂) ₂ -	-(CH ₂) ₃ -	-CH ₂ -	-(CH ₂) ₂ -

Table 20



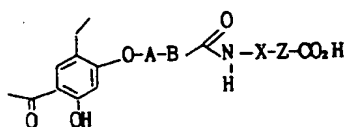
B									
X									
Z	-(CH ₂) ₃ -	-CH ₂ -	-(CH ₂) ₂ -	-(CH ₂) ₃ -	-CH ₂ -	-(CH ₂) ₂ -	-(CH ₂) ₃ -	-CH ₂ -	-(CH ₂) ₂ -

Table 21



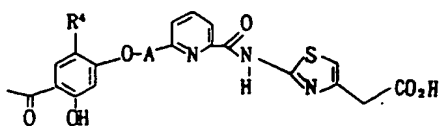
B									
X									
Z	-(CH ₂) ₃ -	-CH ₂ -	-(CH ₂) ₂ -	-(CH ₂) ₃ -	-CH ₂ -	-(CH ₂) ₂ -	-(CH ₂) ₃ -	-CH ₂ -	-(CH ₂) ₂ -

Table 22



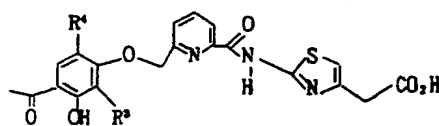
A	-CH ₂ -	-CH ₂ -	-CH ₂ -	-CH ₂ -	-CH ₂ -	-CH ₂ -	-CH ₂ -	-(CH ₂) ₂ -	-(CH ₂) ₃ -
B									
X									
Z	-(CH ₂) ₃ -	-CH ₂ -	-(CH ₂) ₂ -	-(CH ₂) ₃ -	-CH ₂ -	-(CH ₂) ₂ -	-(CH ₂) ₃ -	-CH ₂ -	-CH ₂ -

Table 23



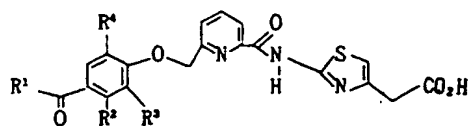
R^4	Et	Et	Et	Me	Et	n-Pr	n-Bu	$-\text{CH}_2\text{CH}=\text{CH}_2$	$\text{CH}_2\text{C}\equiv\text{CH}$
A	$-(\text{CH}_2)_4-$	$-(\text{CH}_2)_5-$	$-\text{CHMe}-$	$-\text{CH}_2-$	$-\text{CH}_2-$	$-\text{CH}_2-$	$-\text{CH}_2-$	$-\text{CH}_2-$	$-\text{CH}_2-$

Table 24



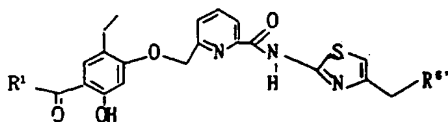
R^3	Me	Et	n-Pr	n-Bu	n-Pentyl	$-\text{CH}_2\text{CH}=\text{CH}_2$	$\text{CH}_2\text{C}\equiv\text{CH}$	Me	Et
R^4	Et	Et	Et	Et	Et	Et	Et	H	H

Table 25



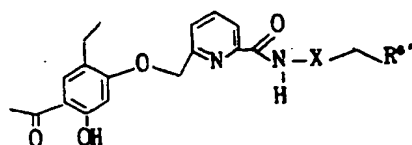
R ¹	Me	Me	Me	Me	Me	Me	Me	Et	n-Pr
R ²	OH	OH	OH	OH	OMe	OEt	O-n-Pr	OH	OH
R ³	i-Pr	i-Bu	n-Bu	n-Pentyl	H	H	H	H	H
R ⁴	H	H	H	H	Et	Et	Et	Et	Et

Table 26



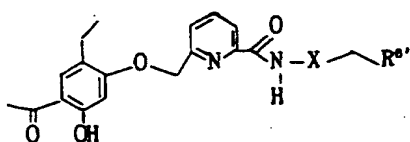
R ¹	n-Bu	n-Pentyl	Me	Me	Me
R ⁶	CO ₂ H	CO ₂ H	$\begin{smallmatrix} \text{O} \\ \parallel \\ \text{CN-CH}_2\text{CO}_2\text{Me} \\ \text{H} \end{smallmatrix}$	$\begin{smallmatrix} \text{O} \\ \parallel \\ \text{CN-(CH}_2\text{)}_2\text{CO}_2\text{Me} \\ \text{H} \end{smallmatrix}$	$\begin{smallmatrix} \text{O} \\ \parallel \\ \text{CN-CH}_2\text{CO}_2\text{H} \\ \text{H} \end{smallmatrix}$

Table 27



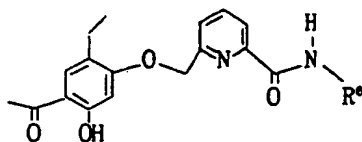
X					
R ⁶	$\begin{array}{c} \text{O} \\ \parallel \\ \text{CN}-(\text{CH}_2)_2\text{CO}_2\text{H} \\ \text{H} \end{array}$	$\begin{array}{c} \text{O} \\ \parallel \\ \text{CN}-\text{CH}_2\text{CO}_2\text{Me} \\ \text{H} \end{array}$	$\begin{array}{c} \text{O} \\ \parallel \\ \text{CN}-(\text{CH}_2)_2\text{CO}_2\text{Me} \\ \text{H} \end{array}$	$\begin{array}{c} \text{O} \\ \parallel \\ \text{CN}-\text{CH}_2\text{CO}_2\text{H} \\ \text{H} \end{array}$	$\begin{array}{c} \text{O} \\ \parallel \\ \text{CN}-(\text{CH}_2)_2\text{CO}_2\text{H} \\ \text{H} \end{array}$

Table 28



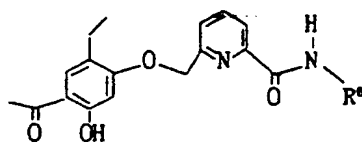
X					
R ⁶	$\begin{array}{c} \text{O} \\ \parallel \\ \text{CN}-(\text{CH}_2)_2\text{CO}_2\text{H} \\ \text{H} \end{array}$	$\begin{array}{c} \text{O} \\ \parallel \\ \text{CN}-\text{CH}(\text{Pr})\text{CO}_2\text{Me} \\ \text{H} \end{array}$	$\begin{array}{c} \text{O} \\ \parallel \\ \text{CN}-\text{CH}(\text{CO}_2\text{H})\text{CO}_2\text{H} \\ \text{H} \end{array}$	$\begin{array}{c} \text{O} \\ \parallel \\ \text{CN}-(\text{CH}_2)_6\text{NH}_2 \\ \text{H} \end{array}$	$\begin{array}{c} \text{O} \\ \parallel \\ \text{CN}-\text{CH}(\text{OH})\text{CO}_2\text{H} \\ \text{H} \end{array}$

Table 29



R ⁶	CH ₂ CO ₂ H	(CH ₂) ₂ CO ₂ H	(CH ₂) ₃ CO ₂ H	(CH ₂) ₄ CO ₂ H	CH ₂ CO ₂ Me
----------------	-----------------------------------	---	---	---	------------------------------------

Table 30







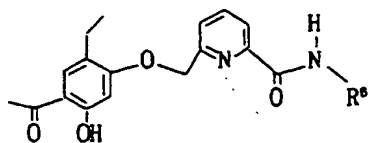
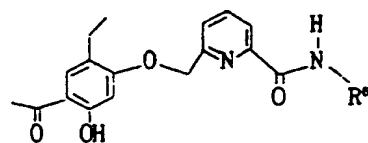
R ⁶	CH ₂ CO ₂ Et	CH ₂ CO ₂ CH ₂ - 	 CO ₂ H	 CO ₂ H	 CO ₂ H
----------------	------------------------------------	---	---	---	---

Table 31



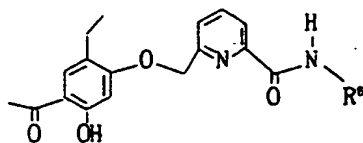
R ⁶					
----------------	--	--	--	--	--

Table 32



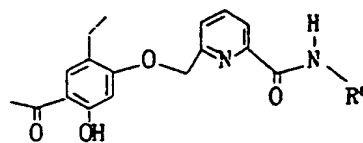
R ⁶					
----------------	--	--	--	--	--

Table 33



R ⁶					
	H	H			

Table 34

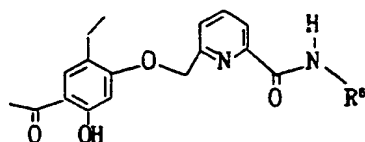


R ⁶					




Table 35

5

10



15

R ⁶	(CH ₂) ₂ CONH ₂	(CH ₂) ₃ CONMe ₂	CH ₂ CON 	CH ₂ CON 	CH ₂ CON 
----------------	---	--	---	--	---

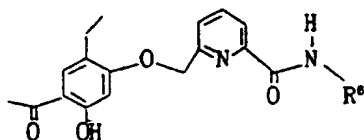
20

25



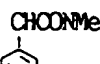
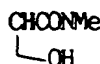

Table 36

30

35



40

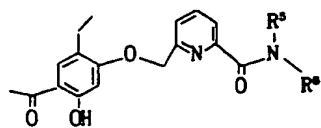
R ⁶					
----------------	---	---	---	--	---

45

50

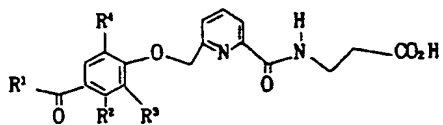
55

Table 37



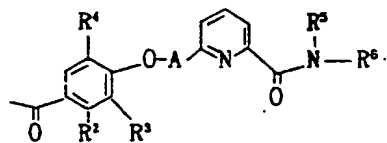
--	--	--	--	--	--

Table 38



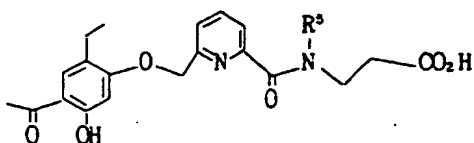
R ¹	Et	n-Pr	Me	Me	Me
R ²	OH	OH	OMe	OEt	OH
R ³	H	H	H	H	n-Pr
R ⁴	Et	Et	Et	Et	H

Table 39



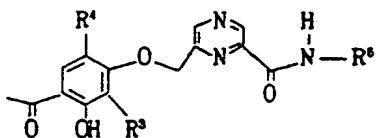
R ²	OH	OMe	OMe	OH	OH
R ³	n-Pr	n-Pr	n-Pr	H	H
R ⁴	H	H	H	Et	Et
A	-CH ₂ -	-CH ₂ -	-CH ₂ -	-(CH ₂) ₂ -	-CH ₂ -
R ⁵	H	H	H	H	Me
R ⁶	CHCO ₂ H CH ₃	CHCO ₂ H CH ₃	(CH ₂) ₂ CO ₂ H	(CH ₂) ₂ CO ₂ H	(CH ₂) ₂ CO ₂ H

Table 40



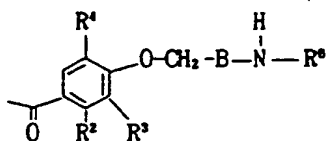
R ⁵	Et	n-Pr	isoBu	sec-Bu	(CH ₂) ₂ OH
----------------	----	------	-------	--------	------------------------------------

Table 41



R ³	H	H	H	H	n-Pr
R ⁴	Et	Et	Et	Et	H
R ⁶	(CH ₂) ₂ CO ₂ H	CHCO ₂ H CH ₃	CHCO ₂ H OH	CHCO ₂ H CH ₂ CO ₂ H	CHCO ₂ H CH ₂ CO ₂ H

Table 42








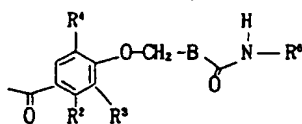
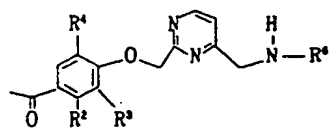
R ²	OMe	OH	OH	OH	OH
R ³	n-Pr	H	H	H	H
R ⁴	H	Et	Et	Et	Et
B					
R ⁶	$\begin{array}{c} \text{CHCO}_2\text{H} \\ \\ \text{CH}_2\text{CO}_2\text{H} \end{array}$	$(\text{CH}_2)_2\text{CO}_2\text{H}$	$\begin{array}{c} \text{CHCO}_2\text{H} \\ \\ \text{CH}_3 \end{array}$	$\begin{array}{c} \text{CHCO}_2\text{H} \\ \\ \text{OH} \end{array}$	$\begin{array}{c} \text{CHCO}_2\text{H} \\ \\ \text{CH}_2\text{CO}_2\text{H} \end{array}$

Table 43



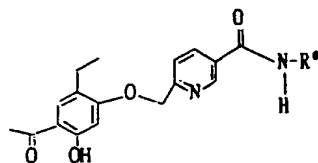
R ²	OH	OMe	OH	OH	OH
R ³	n-Pr	n-Pr	H	H	H
R ⁴	H	H	Et	Et	Et
B					
R ⁶	$\begin{array}{c} \text{CHCO}_2\text{H} \\ \\ \text{CH}_2\text{CO}_2\text{H} \end{array}$	$\begin{array}{c} \text{CHCO}_2\text{H} \\ \\ \text{CH}_2\text{CO}_2\text{H} \end{array}$	$(\text{CH}_2)_2\text{CO}_2\text{H}$	$\begin{array}{c} \text{CHCO}_2\text{H} \\ \\ \text{CH}_3 \end{array}$	$\begin{array}{c} \text{CHCO}_2\text{H} \\ \\ \text{CH}_2\text{OH} \end{array}$

Table 44



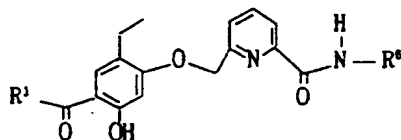
R²	OH	OH	OMe	OH	OH
R³	H	n-Pr	n-Pr	H	H
R⁴	Et	H	H	Et	Et
R⁵	CHCO₂H CH₂CO₂H	CHCO₂H CH₂CO₂H	CHCO₂H CH₂CO₂H	CHCO₂H CH₃	CHCO₂H CH₂OH

Table 45



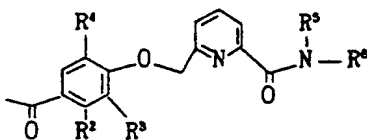
R⁵	CHCO₂H CH(CH₃)₂	CHCO₂H CH₂OH	CHCO₂H CH₂OH	CHCO₂H CH₂OH	CHCH₂CO₂H CH₃
----	-------------------------	----------------------	----------------------	----------------------	-----------------------

Table 46



R ¹	Me	Et	Me	Me	Me
R ⁶	(CH ₂) ₂ OH	(CH ₂) ₃ OH	(CH ₂) ₄ OH	CHCH ₂ OH CH ₃	CHCH ₂ OH CH ₂ CH ₃

Table 47



R ²	OH	O-n-Pr	OH	OH	OH
R ³	Me	H	H	H	H
R ⁴	Me	H	Et	Et	Et
R ⁵	H	H	H	Me	H
R ⁶	(CH ₂) ₂ CO ₂ H	(CH ₂) ₂ CO ₂ H	CH(CH ₂ OH) ₂	CH(CH ₂ OH) ₂	CH ₂ CONHCH ₂ CO ₂ H

Among the leukotriene B₄ antagonists thus obtained, the compound [I] can be converted to a pharmaceutically acceptable salt form. The pharmaceutically acceptable salts of these leukotriene B₄ antagonists can be formed with pharmaceutically acceptable metal cation such as sodium, potassium, magnesium and calcium, ammonium or amine cations.

The preparations of pharmaceutical compositions can be carried out by conventional methods. For

example, leukotriene B₄ antagonists [I] may be mixed with carriers, diluents, lubricants, fillers and/or binders such as lactose, sucrose, calcium phosphate, starch, talcum, casein, magnesium stearate, methyl cellulose, polyglycols, tragacanth and the like, sometimes together with stabilizers and emulsifying agents. The resulting mixture may be processed in a usual manner to tablets, capsules, pills, injections, ointment, 5 suppositories and the like. In a clinical practice, the leukotriene B₄ antagonists [I] can be administered orally, intranasally, intradermally or the like.

The daily dosage may vary depending upon the administration route, symptom, age or weight of the patient, and the usual oral dosage of the active ingredient is between about 1 mg and about 1000 mg daily for human beings.

10

DESCRIPTION OF THE PREFERRED EMBODIMENTS

Practical and preferred embodiments of the present invention are illustrated in the following examples, which are not intended to limit the scope of the invention.

15

Reference Example 1

5-Ethyl-2,4-dihydroxyacetophenone (0.97 g, 5.0 mmol) and methyl 6-bromomethylpyridine-2-carboxylate (1.38 g, 5.8 mmol) were dissolved in an N,N-dimethylformamide solution (50 ml), and anhydrous potassium carbonate (480 mg) was added to the above solution, and the mixture was stirred at room temperature for 16 hours. The reaction mixture was poured into water and extracted with ethyl acetate (100 ml × 3).

20

The extract was dried, concentrated and chromatographed on silica gel to give methyl 6-[(4-acetyl-2-ethyl-5-hydroxyphenoxy)methyl]pyridine-2-carboxylate.

25 Reference Example 2

Methyl 6-[(4-acetyl-2-ethyl-5-hydroxyphenoxy)methyl]pyridine-2-carboxylate (38 mg, 12 mmol) was dissolved in a methanol solution (2 ml), and one normal sodium hydroxide (1 ml) was added to the above solution at 0 °C, and the mixture was stirred at room temperature for 1 hour. One-tenth normal potassium bisulfate was titrated to the above solution until it became pH2. Then, precipitated white crystals were filtered off, and washed with water, and dried to give 6-[(4-acetyl-2-ethyl-5-hydroxyphenoxy)methyl]pyridine-2-carboxylic acid.

30

Reference Example 3

35

3-n-Propyl-2,4-dihydroxyacetophenone (816 mg, 4.2 mmol) was added to a methanol solution (10 ml), sodium metal was added to the solution at 0 °C, and the mixture was stirred for 30 min, and evaporated under reduced pressure, and dried to give a sodium salt of 3-n-propyl-2,4-dihydroxyacetophenone. The salt was dissolved in N,N-dimethylformamide (10 ml), and it was added to a N,N-dimethylformamide solution (10 ml) of methyl-6-bromo-methylpyridine-2-carboxylate (920 mg, 4.0 mmol) at room temperature, and the mixture was stirred for 1 hour.

40

The reaction mixture was poured into water, and normal potassium bisulfate was titrated until it became pH3, and extracted with ethyl acetate (100 ml × 3). The extract was dried, concentrated and chromatographed on silica gel to give methyl 6-[(4-acetyl-3-hydroxy-2-n-propylphenoxy)methyl]pyridine-2-carboxylate.

45

Reference Example 4

According to the procedure of Reference Example 2, 6-[(4-acetyl-3-hydroxy-2-n-propylphenoxy)methyl]pyridine-2-carboxylic acid was obtained by hydrolysis of methyl 6-[(4-acetyl-3-hydroxy-2-n-propylphenoxy)methyl]pyridine-2-carboxylate.

50

Reference Example 5

Anhydrous potassium carbonate (1.0 g) was added to a N,N-dimethylformamide solution (10 ml) of methyl 6-[(4-acetyl-2-ethyl-5-hydroxyphenoxy)methyl]pyridine-2-carboxylate (500 mg, 1.4 mmol) and methyl iodide (5 ml), and the mixture was stirred at 70 °C for 2 hours.

55

The reaction mixture was poured into water and extracted with ethylacetate and washed with saturated aqueous sodium chloride. Then, the extract was dried, concentrated and chromatographed on silica gel to

give methyl 6-[(4-acetyl-2-ethyl-5-methoxyphenoxy)methyl]pyridine-2-carboxylate.

Reference Example 6

- 5 According to the procedure of Reference Example 2, 6-[(4-acetyl-2-ethyl-5-methoxyphenoxy)methyl]-pyridine-2-carboxylic acid was obtained by hydrolysis of methyl 6-[(4-acetyl-2-ethyl-5-methoxy-phenoxy)-methyl]pyridine-2-carboxylate.

Reference Example 7

- 10 According to the procedure of Reference Example 5, methyl 6-[(4-acetyl-2-n-propyl-3-methoxy-phenoxy)methyl]pyridine-2-carboxylate was obtained from methyl 6-[(4-acetyl-3-hydroxy-2-n-propyl-phenoxy)methyl]pyridine-2-carboxylate.

15 Reference Example 8

According to the procedure of Reference Example 2, 6-[(4-acetyl-2-n-propyl-3-methoxyphenoxy)-methyl]pyridine-2-carboxylic acid was obtained by hydrolysis of methyl 6-[(4-acetyl-2-n-propyl-3-methoxyphenoxy)methyl]pyridine-2-carboxylate.

20 Reference Example 9 (a compound included in formula [XVI])

- A mixture of 6-methylpyridine-2-carboxylic acid (13.7 g, 100 mmol) and thionyl chloride (40 ml) was stirred at 70 °C for 1 hour. The mixture was dried, and dichloromethane (40 ml) was added to the residue.
 25 The solution was added to a dichloromethane solution of 2-amino-2-methyl-propanol (36.0 g, 400 mmol), and stirred. The mixture was washed with water, and dried over anhydrous magnesium sulfate. The extract was concentrated and chromatographed on silica gel to give an amide compound. 4,4-Dimethyl-2-oxazoline compound was obtained by reacting the amide compound and thionyl chloride in dichloromethane. 4,4-Dimethyl-2-oxazoline compound was reacted with n-butyl lithium at 78 °C in anhydrous tetrahydrofuran, and
 30 chlorophenyl ether (782 mg, 5 mmol) was added. Purified alkylated compound was treated with ethanol saturated with HCl to give ethyl 6-(3-chloropropyl)-pyridine-2-carboxylate.

Reference Example 10 (a compound included in formula [II])

- 35 According to the procedure of Reference Examples 1,2, 6-[3-(4-acetyl-2-ethyl-5-hydroxyphenoxy)-propyl]pyridine-2-carboxylic acid was obtained from ethyl 6-(3-chloropropyl)pyridine-2-carboxylate and 5-ethyl-2,4-dihydroxyacetophenone.

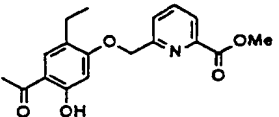
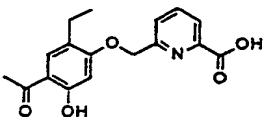
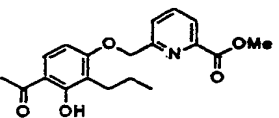
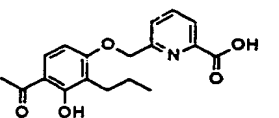
40

45

50

55

Table 48

5		
10	1	
15	2	
25	3	
35	4	
40		
45		
50		

EP 0 516 069 A1

Table 49

		¹ H-NMR	δppm
5	1	(solvent:CDCl ₃) 0.99(3H,t,J = 7.4Hz), 1.62(2H,tq,J = 7.4Hz,J = 7.4Hz), 2.57(3H,s), 2.76(2H,t,J = 7.4Hz), 4.04(3H,s), 5.39(2H,s), 6.46(1H,d,J = 8.9Hz), 7.59(1H,d,J = 8.9Hz), 7.79(1H,d,J = 6.6Hz), 7.92(1H,dd,J = 6.6Hz,J = 7.9Hz), 8.10(1H,d,J = 7.9Hz)	
10	2	(solvent:CDCl ₃) 1.26(3H,t,J = 7.6Hz), 2.59(3H,s), 2.68(2H,q,J = 7.6Hz), 5.30(2H,s), 6.43(1H,s), 7.51(1H,s), 7.78(1H,d,J = 6.9Hz), 8.04(1H,dd,J = 6.9Hz,J = 7.9Hz), 8.22(1H,d,J = 7.9Hz)	
15	3	(solvent:CDCl ₃) 0.99(3H,t,J = 7.4Hz), 1.62(2H,tq,J = 7.4Hz,J = 7.4Hz), 2.57(3H,s), 2.76(2H,t,J = 7.4Hz), 4.04(3H,s), 5.39(2H,s), 6.46(1H,d,J = 8.9Hz), 7.59(1H,d,J = 8.9Hz), 7.79(1H,d,J = 6.6Hz), 7.92(1H,dd,J = 6.6Hz,J = 7.9Hz), 8.10(1H,d,J = 7.9Hz)	
	4	(solvent:CDCl ₃) 0.99(3H,t,J = 7.4Hz), 1.62(2H,tq,J = 7.4Hz,J = 7.4Hz), 2.57(3H,s), 2.76(2H,t,J = 7.4Hz), 5.34(2H,s), 6.45(1H,d,J = 8.9 Hz), 7.60(1H,d,J = 8.9Hz), 7.79(1H,dd,J = 1.0Hz,J = 6.9Hz), 8.04(1H,dd,J = 6.9Hz,J = 7.4Hz), 8.21(1H,dd J = 1.0Hz, J = 7.4Hz)	

20

25

30

35

40

45

50

55

Table 50

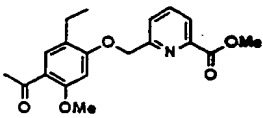
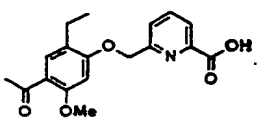
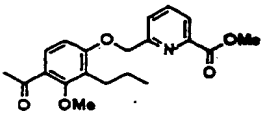
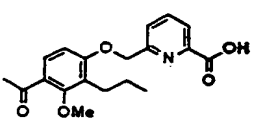
5	
10	5 
15	
20	6 
25	
30	7 
35	
40	8 
45	
50	
55	

Table S1

	¹ H-NMR	δppm
5	5	(solvent:CDCl ₃) 1.24(3H,t,J = 7.6Hz), 2.58(3H,s), 2.70(2H,q,J = 7.6Hz), 3.86(3H,s), 4.04(3H,s), 5.40(2H,s), 7.72(1H,s), 7.79(1H,d,J = 7.9Hz), 7.94(1H,dd,J = 7.9Hz,J = 7.6Hz), 8.11(1H,d,J = 7.6Hz)
10	6	(solvent:CDCl ₃) 1.24(3H,t,J = 7.4Hz), 2.57(3H,s), 2.69(2H,q,J = 7.4Hz), 3.90(3H,s), 5.40(2H,s), 6.64(1H,s), 7.65(1H,s), 7.80(1H,d,J = 7.3Hz), 8.01(1H,dd,J = 7.6Hz,J = 7.6Hz), 8.13(1H,d,J = 7.9Hz)
15	7	(solvent:CDCl ₃) 1.02(3H,t,J = 7.5Hz), 1.66(2H,q,J = 7.6Hz), 2.61(3H,s), 2.75(2H,t,J = 7.8Hz), 3.78(3H,s), 5.31(2H,s), 6.70(1H,d,J = 8.6Hz), 7.56(1H,d,J = 8.9Hz), 7.90(1H,d,J = 7.9Hz), 8.04(1H,dd,J = 7.6Hz,J = 7.9Hz), 8.21(1H,d,J = 7.6Hz)
20	8	(solvent:CDCl ₃) 1.02(3H,t,J = 7.6Hz), 1.65(2H,q,J = 7.7Hz), 2.62(3H,s), 2.75(2H,t,J = 7.8Hz), 3.78(3H,s), 5.31(2H,s), 6.70(1H,d,J = 8.6Hz), 7.56(1H,d,J = 8.9Hz), 7.90(1H,d,J = 7.9Hz), 8.04(1H,dd,J = 7.6Hz,J = 7.9Hz), 8.21(1H,d,J = 7.6Hz)

Example 1

A mixture of 6-[(4-acetyl-2-ethyl-5-hydroxyphenoxy)methyl]pyridine-2-carboxylic acid (63 mg, 0.20 mmol), 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide hydrochloride (40 mg, 0.20 mmol), 1-hydroxybenzotriazole (30 ml, 0.22 mmol), 2-aminothiazole-4-carboxamide (35 mg, 0.24 mg) and triethylamine (20 mg, 0.20 mmol) in a mixed solution of dichloromethane (2 ml) and N,N-dimethylformamide (2 ml) was stirred at room temperature for 44 hours. The reaction mixture was poured into water and extracted with ethyl acetate (80 ml×3). The extract was dried over anhydrous magnesium sulfate, concentrated under reduced pressure and chromatographed on silica gel to give 2-[6-[(4-acetyl-2-ethyl-5-hydroxyphenoxy)-methyl]pyridine-2-carboxamide]thiazol-4-ylcarboxamide.

Example 2~35,62,88,90,92

According to the procedure of Example 1, the compounds (Example 2~ 35,62,88,90,92) were obtained.

Example 36

Ethyl 2-[6-[(4-acetyl-2-ethyl-5-hydroxyphenoxy)methyl]pyridine-2-carboxamide]thiazole-4-ylcarboxylate (24 mg, 0.05 mmol) was suspended in methanol (1.5 ml), followed by addition of one-second normal sodium hydroxide (1.0 ml).

After the solution was stirred for 2 hr, it was made acidic with one-second normal potassium bisulfate. Precipitated crystals were separated by filtration, and washed with water, and dried to give 2-[6-[(4-acetyl-2-ethyl-5-hydroxyphenoxy)methyl]pyridine-2-carboxamide]thiazol-4-ylcarboxylic acid.

Example 37~52,61,87,89,91

According to the procedure of Example 36, the compounds (Example 37 ~52, 61, 87, 89, 91) were obtained.

Example 54~56,64,67,68,70,72,74,76,78,80,82,84,86,94,96,100, 102,104,106,108,112,114,115,116-121,123,126,127,138,141

According to the procedure of Example 1, the title compounds were obtained.

Example 53,57~60,63,65,69,71,73,75,77,79,81,83,85,93,95,99, 101,105,107,111,113,122,130

According to the procedure of Example 36, the title compounds were obtained.

Example 98

Ethyl 2-[6-[(4-acetyl-2-ethyl-5-hydroxyphenoxy)methyl]pyridine-2-carboxamide]pyridine-6-ylcarboxylate (280 mg, 0.60 mM) was dissolved in dichloromethane (5 ml), followed by addition of m-chloroperbenzoic acid (124 mg, 0.72 mM). After being stirred at room temperature for 16 hours, the reaction mixture was washed with aqueous sodium sulfite-sodium bicarbonate, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure to give ethyl 2-[6-[(4-acetyl-2-ethyl-5-hydroxyphenoxy)methyl]pyridine-2-carboxamide]pyridine-N-oxide-6-ylcarboxylate.

Example 110,125,129,131,134,136,139,142

According to the procedure of Example 98, the title compounds were obtained.

Example 97,109,124,128,132,133,135,137,140

According to the procedure of Example 36, the title compounds were obtained.

Example 143~178, 212,214,216,218,222,225,226

According to the procedure of Example 1, the title compounds were obtained.

Example 179~211,213,215,223,224

According to the procedure of Example 36, the title compounds were obtained.

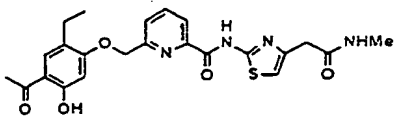
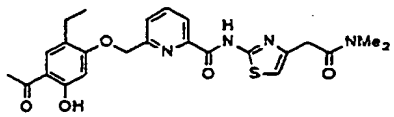
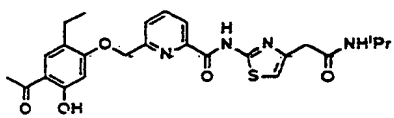
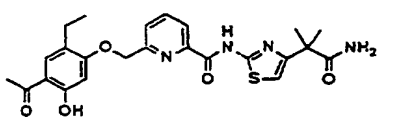
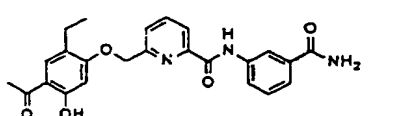
45

EP 0 516 069 A1

Table 53

	¹ H-NMR	δppm
5	1	(solvent:CDCl ₃) 1.28(3H,t,J = 7.6Hz, 2.60(3H,s), 2.71(2H,q,J = 7.6Hz), 5.34(1H,s), 5.55(1H,bs), 6.48(1H,s), 7.05(1H,bs), 7.52(1H,s), 7.77(1H,d,J = 7.3Hz, 9.90(1H,s), 8.04 (1H,dd,J = 6.6Hz, J = 7.3Hz), 8.28(1H,d,J = 7.3Hz), 10.98(1H,bs), 12.70(1H,s)
10	2	(solvent:CDCl ₃) 1.27(3H,J = 7.6Hz), 2.59(3H,s), 2.70(2H,q,J = 7.6Hz), 3.69(2H,s), 5.32(2H,s), 5.43(1H,bs), 6.45(1H,s), 6.60(1H,bs), 6.86(1H,s), 7.51(1H,s), 7.74(1H,d,J = 6.9Hz), 8.02(1H,t,J = 6.9Hz), 8.27(1H,d,J = 6.9Hz), 12.68(1H,s)
15	3	(solvent:CDCl ₃) 1.26(3H,t,J = 7.6Hz), 2.58(3H,s), 2.69(2H,q,J = 7.6Hz), 3.70(2H,s), 3.81(3H,s), 5.39(1H,s), 5.43(1H,bs), 6.46(1H,s), 6.70(1H,bs), 6.88(1H,s), 7.49(1H,s), 7.64(1H,dd,J = 1.0Hz,J = 7.9Hz), 7.79(1H,dd,J = 7.6Hz,J = 7.9Hz), 7.95(1H,dd,J = 1.0Hz,J = 7.6Hz), 12.65(1H,s)
20	4	(solvent:CDCl ₃) 1.26(3H,t,J = 7.6Hz, 1.44(3H,t,J = 6.9Hz), 2.58(3H,s), 2.69(2H,q,J = 7.6Hz), 3.69(2H,s), 4.36(2H,q,J = 6.9Hz) 5.25(1H,s), 5.44(1H,bs), 6.43(1H,s), 6.67(1H,bs), 6.89(1H,s), 7.49(1H,s), 7.64(1H,d,J = 7.9Hz), 7.74(1H,d,J = 6.9Hz), 7.94(1H,dd,J = 6.9Hz),J = 7.9Hz, 12.66(1H,s)
25	5	(solvent:CDCl ₃) 0.78(6H,d,J = 6.6Hz), 1.26(3H,t,J = 7.6Hz), 2.0-2.2(1H,m), 2.58(3H,s), 2.68(2H,q,J = 7.6Hz), 3.66(2H,s), 4.33(2H,d,J = 7.3Hz), 5.21(2H,s), 5.84(1H,bs), 6.42(1H,s), 6.60(1H,bs), 6.88(1H,s), 7.49(1H,s), 7.62(1H,d,J = 7.6Hz), 7.74(1H,d,J = 7.9Hz), 7.93(1H,dd,J = 6Hz,J = 7.9Hz), 12.66(1H,s)

Table 54

Ex. No.	Structural formula
6	 <chem>CCc1cc(O)c(cc1C(=O)O)OCc2ccncc2C(=O)Nc3cc(C(=O)NC)ns3</chem>
7	 <chem>CCc1cc(O)c(cc1C(=O)O)OCc2ccncc2C(=O)Nc3cc(C(=O)NC)ns3</chem>
8	 <chem>CCc1cc(O)c(cc1C(=O)O)OCc2ccncc2C(=O)Nc3cc(C(=O)NC)ns3</chem>
9	 <chem>CCc1cc(O)c(cc1C(=O)O)OCc2ccncc2C(=O)Nc3cc(C(=O)NC)ns3</chem>
10	 <chem>CCc1cc(O)c(cc1C(=O)O)OCc2ccncc2C(=O)Nc3cc(C(=O)NC)ns3</chem>

EP 0 516 069 A1

Table 55

	¹ H-NMR	δppm
5	6	(solvent:CDCl ₃) 1.28(3H,t,J = 7.6Hz), 2.59(3H,s), 2.70(2H,q,J = 7.6Hz), 2.84(3H,d,J = 5.0Hz), 3.67(2H,s), 5.33(2H,s), 6.45(1H,s), 6.48(1H,bs), 6.85(1H,s), 7.51(1H,s), 7.74(1H,d,J = 6.6Hz), 8.02(1H,t,J = 6.6Hz), 8.27(1H,d,J = 6.6Hz), 11.06(1H,bs), 12.70(1H,s)
10	7	(solvent:CDCl ₃) 1.27(3H,t,J = 7.6Hz), 2.59(3H,s), 2.70(2H,q,J = 7.6Hz), 3.01(3H,s), 3.11(1H,s), 3.83(2H,s), 5.28(2H,s), 6.43(1H,s), 6.86(1H,b), 7.51(1H,s), 7.72(1H,dd,J = 1.0Hz,J = 7.9Hz), 8.00(1H,t,J = 7.9Hz), 8.25(1H,dd,J = 1.0Hz,J = 7.9Hz), 11.08(1H,bs), 12.70(1H,s)
15	8	(solvent:CDCl ₃) 1.15(6H,d,J = 6.6Hz), 1.27(3H,t,J = 7.6Hz), 2.59(3H,s), 2.70(2H,q,J = 7.6Hz), 3.63(2H,s), 4.0-4.2(1H,m), 5.32(1H,s), 6.06(1H,bs), 6.45(1H,s), 6.85(1H,s), 7.51(1H,s), 7.74(1H,d,J = 7.9Hz), 8.02(1H,t,J = 7.9Hz), 8.27(1H,d,J = 7.9Hz), 11.06(1H,bs), 12.70(1H,s)
20	9	(solvent:CDCl ₃) 1.27(3H,t,J = 7.6Hz), 1.31(3H,s), 1.34(3H,s), 2.59(3H,s), 2.70(2H,q,J = 7.6Hz), 3.1-3.2(1H,m), 5.30(2H, s), 6.44(1H,s), 6.62(1H,s), 7.51(1H,s), 7.71(1H,d,J = 7.9Hz), 7.99(1H,dd,J = 6.6Hz,J = 7.9Hz), 8.26(1H,d,J = 6.6Hz), 11.05(1H,bs), 12.67(1H,s)
	10	(solvent:CDCl ₃) 1.23(3H,t,J = 7.6Hz), 2.60(3H,s), 2.65(2H,q,J = 7.6Hz), 5.49(2H,s), 6.64(1H,s), 7.35-7.55(2H,m), 7.6-7.8(3H,m), 8.0-8.3(5H,m), 10.59(1H,bs), 12.60(1H,s)

25

30

35

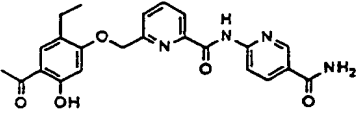
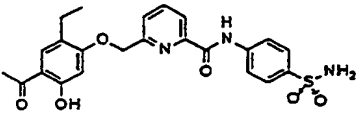
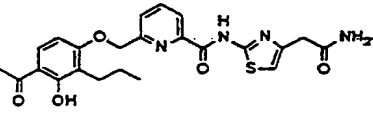
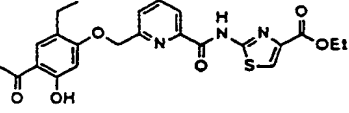
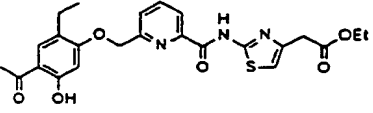
40

45

50

55

Table 56

Ex. No.	Structural formula
1 1	
1 2	
1 3	
1 4	
1 5	

EP 0 516 069 A1

Table 57

		¹ H-NMR	δppm
5	11	(solvent:CDCl ₃) 1.22(3H,t,J = 7.6Hz), 2.58(3H,s), 2.67(2H,q,J = 7.6Hz), 5.49(1H,s), 6.64(1H,s), 7.53(1H,bs), 7.71(1H,s), 7.80-7.85(1H,m), 8.1-8.4(5H,m), 8.85-8.90(1H,m), 10.63(1H,bs), 12.56(1H,s)	
	12	(solvent:CDCl ₃) 1.20(3H,t,J = 7.6Hz), 2.58(2H,s), 2.64(2H,q,J = 7.6Hz), 5.47(2H,s), 6.62(1H,s), 7.30(2H,s), 7.71(1H,s), 7.75-7.90(3H,m), 8.0-8.2(4H,m), 10.75(1H,bs), 12.56(1H,s)	
10	13	(solvent:CDCl ₃) 1.00(3H,t,J = 7.4Hz), 1.63(2H,tq,J = 7.4Hz,J = 7.4Hz), 2.58(3H,s), 2.77(2H,t,J = 7.4Hz), 3.69(2H,s), 5.36(2H,s), 5.40(1H,bs), 6.47(1H,d,J = 9.2Hz), 6.50(1H,bs), 6.87(1H,s), 7.62(1H,d, J = 9.2Hz), 7.76(1H,d,J = 7.9Hz, 8.02(1H,dd,J = 7.9Hz, J = 7.9Hz), 8.26(1H,d,J = 7.9Hz)	
15	14	(solvent:CDCl ₃) 1.27(3H,t,J = 7.6Hz), 1.43(3H,t,J = 7.1Hz), 2.59(3H,s), 2.70(2H,q,J = 7.6Hz), 4.45(2H,q,J = 7.1Hz), 5.28(1H,s) 6.43(1H,s), 7.52(1H,s), 7.73(1H,d,J = 7.9Hz), 7.94(1H,d,J = 0.7Hz) 8.01(1H,t,J = 7.9Hz), 8.25(1H,d,J = 7.9Hz), 11.32(1H,bs), 12.66(1H,s)	
20	15	(solvent:CDCl ₃) 1.27(3H,t,J = 7.6Hz), 1.30(3H,t,J = 7.3Hz), 2.59(3H,s), 2.70(2H,q,J = 7.6Hz), 3.76(2H,d,J = 0.7Hz), 4.22(2H,q,J = 7.3Hz), 5.28(1H,s), 6.43(1H,s), 6.90(1H,d,J = 0.7 Hz), 7.51(1H,s), 7.72(1H,d,J = 7.9Hz), 8.00(1H,dd,J = 7.6Hz,J = 7.9Hz), 8.25(1H,d,J = 7.6Hz), 11.11(1H,bs), 12.67(1H,s)	

25

30

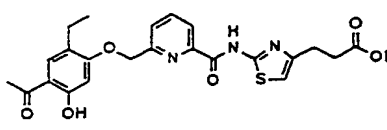
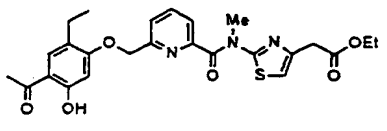
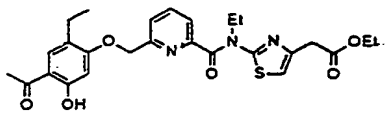
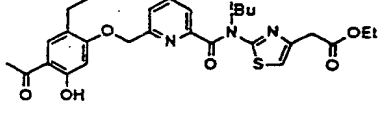
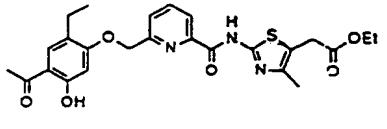
35

40

45

50

55

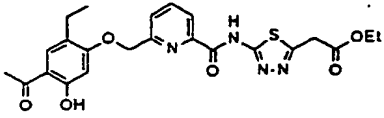
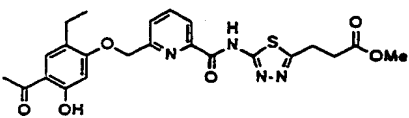
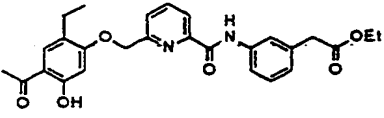
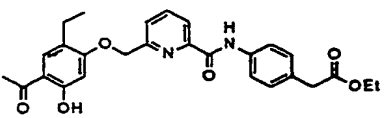
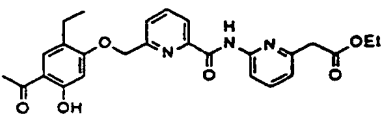
Ex. No.	Structural formula
1 6	
1 7	
1 8	
1 9	
2 0	

EP 0 516 069 A1

Table 59

	¹ H-NMR	δppm
5	16	(solvent:CDCl ₃) 1.25(3H,t,J = 7.3Hz), 1.27(3H,t,J = 7.4Hz), 2.59(3H,s), 2.65-2.80(4H,m), 3.05(2H,t,J = 7.3Hz), 4.15(2H,q,J = 7.3Hz), 5.30(2H,s), 6.44(1H,s), 6.69(1H,s), 7.51 (1H,s), 7.71(1H,d,J = 7.7Hz), 7.97(1H,t,J = 7.7Hz), 8.24(1H,d,J = 7.7Hz), 11.05(1H,bs), 12.67(1H,s)
10	17	(solvent:CDCl ₃) 1.27(3H,t,J = 7.6Hz), 1.43(3H,t,J = 7.1Hz), 2.59(3H,s), 2.70(2H,q,J = 7.6Hz), 4.45(2H,q,J = 7.1Hz), 5.28(1H,s) 6.43(1H,s), 7.52(1H,s), 7.73(1H,d,J = 7.9Hz), 7.94(1H,d,J = 0.7Hz) , 8.01(1H,t,J = 7.9Hz), 8.25(1H,d,J = 7.9Hz), 11.32(1H,bs), 12.66(1H,s)
15	18	(solvent:CDCl ₃) 1.26(3H,t,J = 7.6Hz), 1.28(3H,t,J = 7.1Hz), 1.40(3H,t,J = 6.9Hz), 2.58(3H,s),2.69(2H,q,J = 7.6Hz), 3.76(2H,d,J = 0.7Hz), 4.20(2H,q,J = 7.1Hz), 4.32(2H,q,J = 6.9Hz), 5.25(1H,s), 6.44(1H,s), 6.92(1H,s), 7.49(1H,s), 7.62(1H,d,J = 7.6Hz), 7.70(1H,d,J = 6.9Hz), 7.92(1H,dd,J = 6.9Hz,J = 7.6Hz), 12.65(1H,s)
20	19	(solvent:CDCl ₃) 0.76(6H,d,J = 6.6Hz), 1.26(3H,t,J = 7.6Hz), 1.27(3H,t,J = 7.1Hz), 2.0-2.2(1H,m), 2.58(3H,s), 2.68(2H,q,J = 7.6Hz), 3.74(2H,s), 4.18(2H,d,J = 7.1Hz), 4.28(2H,d,J = 6.9Hz), 5.21(2H,s), 6.43(1H,s), 6.91(1H,s), 7.49(1H,s), 7.58(1H,d,J = 7.9Hz), 7.71(1H,d,J = 7.9Hz), 7.90(1H,t,J = 7.9Hz), 12.63(1H,s)
25	20	(solvent:CDCl ₃) 1.27(3H,t,J = 7.4Hz), 1.29(3H,t,J = 7.3Hz), 2.33(3H,s), 2.59(3H,s), 2.69(2H,q,J = 7.4Hz), 3.73(2H,s), 4.20(2H,q,J = 7.3Hz), 5.27(2H,s), 6.43(1H,s), 7.51(1H,s), 7.71(1H,d,J = 7.9Hz), 7.99(1H,t,J = 7.9Hz), 8.24(1H,d,J = 7.9Hz), 10.98(1H,bs), 12.67(1H,s)

Table 60

Ex. No.	Structural formula
2 1	
2 2	
2 3	
2 4	
2 5	

EP 0 516 069 A1

Table 61

	¹ H-NMR	δppm
5	21	(solvent:CDCl ₃) 1.27(3H,t,J = 7.6Hz), 1.32(3H,t,J = 7.1Hz), 2.59(3H,s), 2.71(2H,q,J = 7.1Hz), 4.16(2H,s), 4.27(2H,q,J = 7.6Hz) 5.32(2H,s), 6.44(1H,s), 7.52(1H,s), 7.75(1H,d,J = 7.6Hz), 8.02(1H,t,J = 7.6Hz), 8.26(1H,d,J = 7.6Hz), 11.21(1H,bs), 12.67(1H,s)
10	22	(solvent:CDCl ₃) 1.27(3H,t,J = 7.4Hz), 2.58(3H,s), 2.70(2H,q,J = 7.4Hz), 2.93(2H,t,J = 7.3Hz), 3.40(2H,t,J = 7.3Hz), 3.73(3H,s), 5.32(2H,s), 6.43(1H,s), 7.51(1H,s), 7.75(1H,d,J = 7.9Hz), 8.01(1H,t,J = 7.9Hz), 8.24(1H,d,J = 7.9Hz), 11.18(1H,bs), 12.66(1H,s)
15	23	(solvent:CDCl ₃) 1.27(3H,t,J = 7.3Hz), 1.27(3H,t,J = 7.3Hz), 2.59(3H,s), 2.70(2H,q,J = 7.3Hz), 3.66(2H,s), 4.17(2H,q,J = 7.3Hz) 5.32(2H,s), 6.52(1H,s), 7.0-7.1(1H,m), 7.3-7.4(1H,m), 7.51(1H,s), 7.65-7.7(2H,m), 7.97(1H,t,J = 7.7Hz), 8.26(1H,dd,J = 1.0Hz,J = 7.7Hz), 9.92(1H,bs), 12.68(1H,s)
20	24	(solvent:CDCl ₃) 1.26(3H,t,J = 7.1Hz), 1.27(3H,t,J = 7.6Hz), 2.59(3H,s), 2.70(2H,q,J = 7.6Hz), 3.62(2H,s), 4.16(2H,q,J = 7.1Hz) 5.32(2H,s), 6.51(1H,s), 7.32(1H,d,J = 8.6Hz), 7.51(1H,s), 7.67(1H,d,J = 7.3Hz), 7.75(1H,d,J = 8.6Hz), 7.98(1H,dd,J = 7.3Hz,J = 7.6Hz), 8.27(1H,d,J = 7.6Hz), 9.90(1H,bs), 12.68(1H,s)
25	25	(solvent:CDCl ₃) 1.28(3H,t,J = 7.6Hz), 1.29(3H,t,J = 7.3Hz), 2.59(3H,s), 2.71(2H,q,J = 7.6Hz), 3.80(2H,s), 4.21(2H,q,J = 7.3Hz) 5.34(2H,s), 6.47(1H,s), 7.09(1H,d,J = 6.9Hz), 7.51(1H,s), 7.65-7.85(2H,m), 7.97(1H,t,J = 7.6Hz), 8.26(1H,t,J = 7.6Hz), 8.30(1H,t,J = 7.6Hz), 10.37(1H,bs), 12.66(1H,s)

25

30

35

40

45

50

55

Table 62

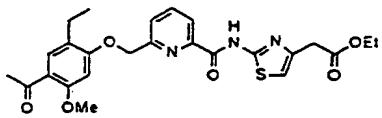
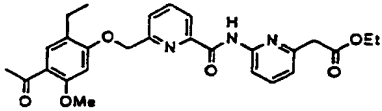
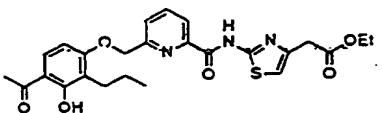
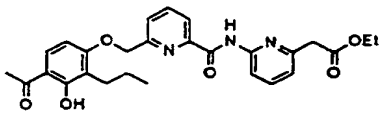
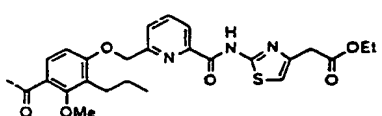
Ex. No.	Structural formula
2 6	
2 7	
2 8	
2 9	
3 0	

Table 63

	¹ H-NMR	δppm
26	(solvent:CDCl ₃) 1.25(3H,t,J = 7.3Hz), 1.30(3H,t,J = 7.3Hz), 2.59(3H,s), 2.71(2H,q,J = 7.5Hz), 3.77(2H,s), 3.92(2H,s), 4.22(2H,q,J = 7.5Hz), 5.32(2H,s), 6.50(1H,s), 6.91(1H,s), 7.73(1H,s), 7.80(1H,d,J = 7.6Hz), 8.03(1H,dd,J = 7.9Hz,J = 7.6Hz), 8.24(1H,d,J = 7.6Hz), 11.18(1H,s)	
27	(solvent:CDCl ₃) 1.26(3H,t,J = 7.6Hz), 1.28(3H,t,J = 7.4Hz), 2.59(3H,s), 2.72(2H,q,J = 7.5Hz), 3.80(2H,s), 3.92(3H,s), 4.21(2H,q,J = 7.5Hz), 5.38(2H,s), 6.57(1H,s), 7.10(1H,dd,J = 7.0Hz,J = 0.7Hz), 7.73(1H,s), 7.76(1H,dd,J = 8.3Hz,J = 7.9Hz), 7.77(1H,dd,J = 7.9Hz,J = 1.0Hz), 8.00(1H,dd,J = 7.6Hz,J = 7.9Hz), 8.27(1H,dd,J = 7.9Hz,J = 1.0Hz), 8.37(1H,d,J = 8.3Hz), 10.40(1H,s)	
28	(solvent:CDCl ₃) 1.00(3H,t,J = 7.4Hz), 1.30(3H,t,J = 7.1Hz), 1.63(2H,tq,J = 7.9Hz,J = 7.3Hz), 2.58(3H,s), 2.77(2H,t,J = 7.6Hz), 3.77(2H,s), 4.22(2H,q,J = 7.0Hz), 5.32(1H,s), 6.46(1H,d,J = 8.9Hz), 6.91(1H,s), 7.62(1H,d,J = 8.9Hz), 7.74(1H,d,J = 7.9Hz), 8.00(1H,dd,J = 7.6Hz,J = 7.9Hz), 8.24(1H,dd,J = 7.6Hz,J = 0.6Hz)	
29	(solvent:CDCl ₃) 1.00(3H,t,J = 7.4Hz), 1.29(3H,t,J = 7.2Hz), 1.64(2H,tq,J = 7.6Hz,J = 7.2Hz), 2.58(3H,s), 2.78(2H,t,J = 7.2Hz), 3.81(2H,s), 4.21(2H,q,J = 7.0Hz), 5.38(2H,s), 6.50(1H,d,J = 8.9Hz), 7.10(1H,dd,J = 7.3Hz,J = 0.7Hz), 7.62(1H,d,J = 8.9Hz), 7.70(1H,d,J = 7.9Hz), 7.76(1H,dd,J = 8.0Hz,J = 7.9Hz), 7.97(1H,dd,J = 7.9Hz,J = 7.6Hz), 8.25(1H,d,J = 6.9Hz), 8.36(1H,d,J = 7.6Hz)	
30	(solvent:CDCl ₃) 1.03(3H,t,J = 7.3Hz), 1.64(2H,tq,J = 7.6Hz,J = 7.8Hz), 2.59(3H,s), 2.74(2H,t,J = 8.0Hz), 3.78(3H,s), 3.82(2H,s), 5.31(2H,s), 6.71(1H,d,J = 8.9Hz), 6.83(1H,s), 7.53(1H,d,J = 8.9Hz), 7.70(1H,d,J = 7.6Hz), 7.97(1H,dd,J = 7.6Hz,J = 7.9Hz), 8.19(1H,d,J = 7.6Hz)	

Table 64

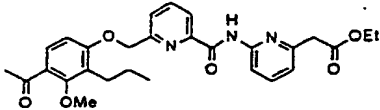
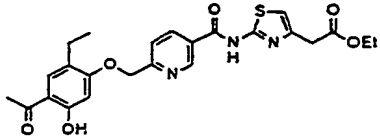
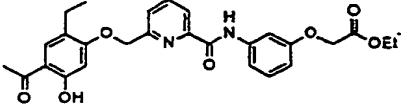
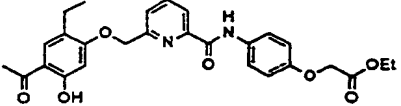
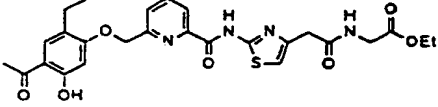
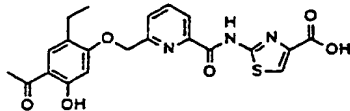
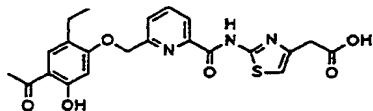
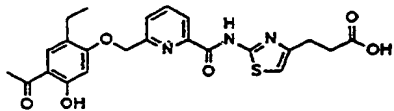
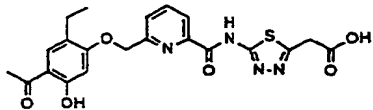
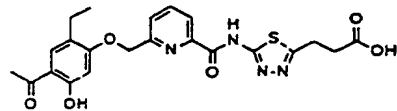
Ex. No.	Structural formula
3 1	
3 2	
3 3	
3 4	
3 5	

Table 65

	¹ H-NMR	δppm
31	(solvent:CDCl ₃) 1.03(3H,t,J = 7.3Hz), 1.65(2H,tq,J = 7.6Hz,J = 7.9Hz), 2.63(3H,s), 2.76(2H,t,J = 7.6Hz), 3.79(3H,s), 3.90(2H,s), 5.37(2H,s), 6.81(1H,d,J = 8.6Hz), 7.06(1H,d,J = 7.6Hz), 7.59(1H,d,J = 8.9Hz), 7.75(1H,d,J = 6.9Hz), 7.83(1H,dd,J = 7.9Hz,J = 7.9Hz), 8.01(1H,dd,J = 7.9Hz,J = 7.9Hz), 8.28(1H,d,J = 6.9Hz), 8.37(1H,d,J = 7.9Hz)	
32	(solvent:CDCl ₃) 1.27(3H,t,J = 7.6Hz), 1.28(3H,t,J = 7.1Hz), 2.59(3H,s), 2.71(2H,q,J = 7.6Hz), 3.72(2H,s), 4.17(2H,q,J = 7.3Hz), 5.32(2H,s), 6.43(1H,s), 6.89(1H,s), 7.51(1H,s), 7.67(1H,dd,J = 0.7Hz,J = 8.2Hz), 8.29(1H,dd,J = 2.3Hz,J = 8.2Hz), 9.14(1H,dd,J = 0.7Hz,J = 2.3Hz), 9.58(1H,bs), 12.66(1H,s)	
33	(solvent:CDCl ₃) 1.27(3H,t,J = 7.6Hz), 1.32(3H,t,J = 7.3Hz), 2.59(3H,s), 2.70(2H,q,J = 7.6Hz), 4.30(2H,q,J = 7.3Hz), 4.68(2H,s), 5.32(2H,s), 6.51(1H,s), 6.70-6.80(1H,m), 7.25-7.35(2H,m), 7.51(1H,s), 7.55-7.65(1H,m), 7.68(1H,d,J = 7.6Hz), 7.98(1H,dd,J = 6.6Hz,J = 7.6Hz), 8.26(1H,d,J = 6.6Hz), 9.90(1H,bs), 12.67(1H,s)	
34	(solvent:CDCl ₃) 1.27(3H,t,J = 7.6Hz), 1.31(3H,t,J = 7.3Hz), 2.59(3H,s), 2.70(2H,q,J = 7.6Hz), 4.26(2H,q,J = 7.3Hz), 4.63(2H,s), 5.31(2H,s), 6.51(1H,s), 6.96(2H,d,J = 9.1Hz), 7.51(1H,s), 7.66(1H,d,J = 8.6Hz), 7.71(2H,d,J = 9.1Hz), 7.97(1H,dd,J = 7.6Hz,J = 8.6Hz), 8.26(1H,d,J = 7.6Hz), 9.82(1H,s), 12.67(1H,s)	
35	(solvent:CDCl ₃) 1.27(3H,t,J = 7.3Hz), 1.27(3H,t,J = 7.3Hz), 2.59(3H,s), 2.70(2H,q,J = 7.6Hz), 3.73(2H,s), 4.07(2H,d,J = 5.3Hz), 4.20(2H,q,J = 7.3Hz), 5.32(2H,s), 6.45(1H,s), 6.88(1H,s), 7.03(1H,b), 7.51(1H,s), 7.74(1H,dd,J = 1.0Hz, J = 7.6Hz), 8.01(1H,dd,J = 7.6Hz,J = 7.9Hz), 8.25(1H,dd,J = 1.0Hz,J = 7.9Hz), 11.08(1H,bs), 12.67(1H,s)	

Table 66

Ex. No.	Structural formula
3 6	
3 7	
3 8	
3 9	
4 0	

EP 0 516 069 A1

Table 67

		¹ H-NMR	δppm
5	36	(solvent:DMSO-d ₆) 1.20(3H,t,J = 7.6Hz), 2.59(3H,s), 2.63(2H,q,J = 7.6Hz), 5.44(2H,s), 6.71(1H,s), 7.45(1H,s), 7.66(1H,s), 7.7-7.8(1H,m), 8.10-8.20(2H,m), 12.60(1H,bs)	
	37	(solvent:DMSO-d ₆) 1.21(3H,t,J = 6Hz), 2.58(3H,s), 2.65(2H,q,J = 7.6Hz), 3.67(2H,s), 5.46(2H,s), 6.63(1H,s), 7.11(1H,s), 7.70(1H,s), 7.78(1H,dd,J = 1.3Hz,J = 7.3Hz), 12.04(1H,bs), 12.55(1H,s)	
10	38	(solvent:DMSO-d ₆) 1.21(3H,t,J = 7.4Hz), 2.59(3H,s), 2.55-2.75(4H,m), 2.89(2H,t,J = 7.6Hz), 5.47(2H,s), 6.63(1H,s), 6.95 (1H,s), 7.70(1H,s), 7.78(1H,d,J = 7.3Hz), 8.10-8.20(2H,m), 11.94(1H,bs), 12.57(1H,s)	
	39	(solvent:DMSO-d ₆) 1.21(3H,t,J = 7.4Hz), 2.58(3H,s), 2.65(2H,q,J = 7.4Hz), 4.15(2H,s), 5.47(2H,s), 6.63(1H,s), 7.70(1H,s), 7.80(1H,d,J = 6.9Hz), 8.10-8.20(2H,m), 12.50(1H,bs), 12.56(1H,s)	
15	40	(solvent:DMSO-d ₆) 1.21(3H,t,J = 7.4Hz), 2.59(3H,s), 2.55-2.75(4H,m), 2.89(2H,t,J = 7.6Hz), 5.47(2H,s), 6.63(1H,s), 6.95(1H,s), 7.70(1H,s), 7.78(1H,d,J = 7.3Hz), 8.10-8.20 (2H,m), 11.94(1H,bs), 12.57(1H,s)	

20

25

30

35

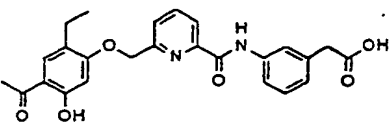
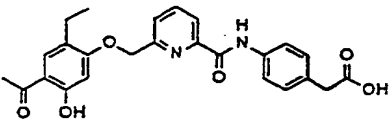
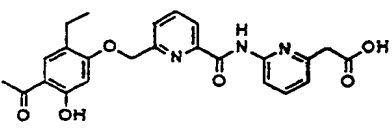
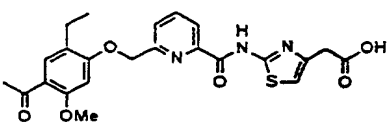
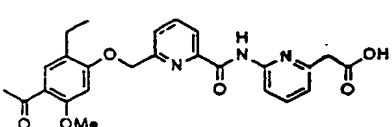
40

45

50

55

Table 68

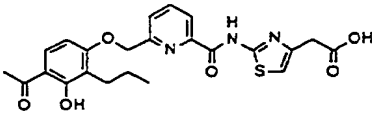
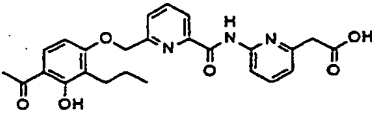
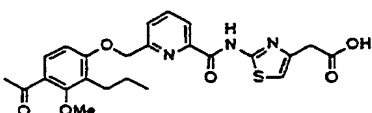
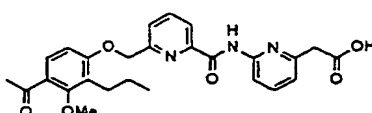
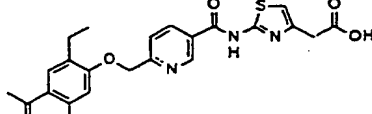
Ex. No.	Structural formula
4 1	
4 2	
4 3	
4 4	
4 5	

EP 0 516 069 A1

Table 69

	¹ H-NMR	δppm
5	41	(solvent:DMSO-d ₆) 1.20(3H,t,J = 7.6Hz), 2.58(3H,s), 2.65(2H,q,J = 7.6Hz), 3.58(1H,s), 5.47(2H,s), 6.63(1H,s), 7.04(1H,d,J = 7.9Hz), 7.33(1H,m), 7.7-7.8(4H,m), 8.1-8.2(2H,m), 10.41(1H,s), 12.56(1H,s)
10	42	(solvent:DMSO-d ₆) 1.20(3H,t,J = 7.6Hz), 2.58(3H,s), 2.65(2H,q,J = 7.6Hz), 5.46(2H,s), 6.62(1H,s), 7.27(2H,d,J = 8.2Hz) 7.65-7.85(4H,m), 8.05-8.20(2H,m), 8.10-8.20(2H,m), 10.40(1H,s), 12.56(1H,bs)
15	43	(solvent:DMSO-d ₆) 1.23(3H,t,J = 7.6Hz), 2.58(3H,s), 2.67(2H,q,J = 7.6Hz), 3.71(2H,s), 5.49(2H,s), 6.65(1H,s), 7.17(1H,d,J = 6.9Hz), 7.69(1H,s), 7.75-7.95(2H,m), 8.10-8.20 (3H,m), 10.33(1H,s), 12.55(1H,bs)
20	44	(solvent:CDCl ₃) 1.25(3H,t,J = 7.4Hz), 2.57(3H,s), 2.70(2H,q,J = 7.2Hz), 3.83(2H,s), 3.89(3H,s), 5.35(2H,s), 6.52(1H,s), 6.88(1H,s), 7.70(1H,s), 7.81(1H,d,J = 7.6Hz), 8.03(1H,dd,J = 7.9Hz,J = 7.6Hz), 8.24(1H,d,J = 7.6Hz)
25	45	(solvent:CDCl ₃) 1.26(3H,t,J = 6.7Hz), 2.59(3H,s), 2.72(2H,q,J = 6.9Hz), 3.91(2H,s), 3.93(3H,s), 5.39(2H,s), 6.55(1H,s), 7.07(1H,d,J = 7.3Hz), 7.74(1H,s), 7.83(1H,d,J = 6.6Hz) 7.86(1H,dd,J = 7.8Hz,J = 7.6Hz), 8.04(1H,dd,J = 7.9Hz,J = 7.9Hz), 8.29(1H,d,J = 6.6Hz), 8.41(1H,d,J = 8.3Hz)
30		
35		
40		
45		
50		
55		

Table 70

Ex. No.	Structural formula
4 6	
4 7	
4 8	
4 9	
5 0	

EP 0 516 069 A1

Table 71

	¹ H-NMR	δppm
5	46	(solvent:DMSO-d ₆) 0.92(3H,t,J = 7.3Hz), 1.55(2H,tq,J = 6.9Hz, J = 7.7Hz), 2.52(3H,s), 2.67(2H,t,J = 7.6Hz), 3.67(2H,s), 5.50(2H,s), 6.77(1H,d,J = 9.2Hz), 7.11(1H,s), 7.76(1H,d,J = 7.2Hz) 7.81(1H,d,J = 8.9Hz), 8.11(1H,dd,J = 7.6Hz,J = 7.6Hz), 8.13(1H,d,J = 7.6Hz)
10	47	(solvent:CDCl ₃) 1.00(3H,t,J = 7.4Hz), 1.64(2H,tq,J = 7.6Hz, J = 7.3Hz), 2.59(3H,s), 2.78(2H,t,J = 7.6Hz), 3.91(2H,s), 5.40(2H,s), 6.55(1H,d,J = 8.9Hz), 7.07(1H,d,J = 6.6Hz), 7.63(1H,d,J = 8.2Hz), 7.77(1H,d,J = 6.9Hz), 7.85(1H,dd,J = 7.9Hz,J = 7.9Hz), 8.02(1H,dd,J = 7.6Hz,J = 7.9Hz), 8.27(1H,d,J = 6.9Hz), 8.39(1H,d,J = 8.3Hz)
15	48	(solvent:CDCl ₃) 1.03(3H,t,J = 7.3Hz), 1.64(2H,tq,J = 7.6Hz,J = 7.8Hz), 2.59(3H,s), 2.74(2H,t,J = 8.0Hz), 3.78(3H,s), 3.82(2H,s) 5.31(2H,s), 6.71(1H,d,J = 8.9Hz), 6.83(1H,s), 7.53(1H,d,J = 8.9Hz), 7.70(1H,d,J = 7.6Hz), 7.97(1H,dd,J = 7.6Hz,J = 7.9Hz), 8.19(1H,d,J = 7.6Hz)
20	49	(solvent:CDCl ₃) 1.03(3H,t,J = 7.3Hz), 1.65(2H,tq,J = 7.6Hz,J = 7.9Hz), 2.63(3H,s), 2.76(2H,t,J = 7.6Hz), 3.79(3H,s), 3.90(2H,s), 5.37(2H,s), 6.81(1H,d,J = 8.6Hz), 7.06(1H,d,J = 7.6Hz), 7.59(1H,d, J = 8.9Hz), 7.75(1H,d,J = 6.9Hz), 7.83(1H,dd,J = 7.9Hz, J = 7.9Hz), 8.01(1H,dd,J = 7.9Hz,J = 7.9Hz), 8.28(1H,d,J = 6.9Hz) 8.37(1H,d,J = 7.9Hz)
	50	(solvent:DMSO-d ₆) 1.20(3H,t,J = 7.6Hz), 2.58(3H,s), 2.64(2H,q,J = 7.6Hz), 3.66(2H,s), 5.38(2H,s), 6.57(1H,s), 7.06(1H,s), 7.66(1H,d,J = 8.6Hz), 7.69(1H,s), 8.48(1H,dd,J = 2.0Hz,J = 8.6Hz), 9.22(1H,d,J = 2.0Hz), 12.54(1H,s)

25

30

35

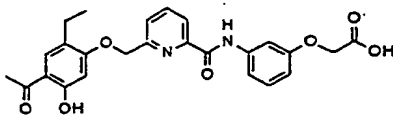
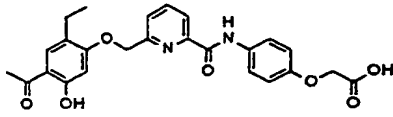
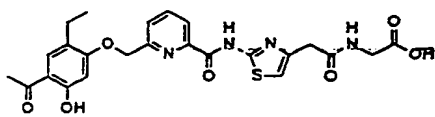
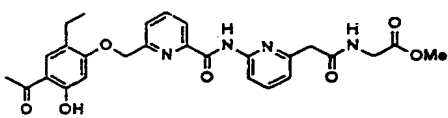
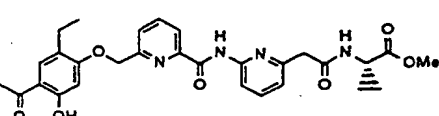
40

45

50

55

Table 72

Ex. No.	Structural formula
5 1	
5 2	
5 3	
5 4	
5 5	

EP 0 516 069 A1

Table 73

		¹ H-NMR	δppm
5	51	(solvent:DMSO-d ₆) 1.19(3H,t,J = 7.6Hz), 2.58(3H,s), 2.64(2H,q,J = 7.6Hz), 4.64(2H,s), 5.45(2H,s), 6.62(1H,s), 6.93(2H,d,J = 8.2Hz), 7.65-7.85(4H,m), 8.05-8.20(2H,m), 10.35(1H,s), 12.55(1H,s)	
	52	(solvent:DMSO-d ₆) 1.20(3H,t,J = 7.6Hz), 2.58(3H,s), 2.64(2H,q,J = 7.6Hz), 4.66(2H,s), 5.46(2H,s), 6.62(1H,s), 6.65-6.75(1H,m), 7.20-7.80(5H,m), 8.05-8.20(2H,m), 10.41(1H,s) 12.56(1H,s),	
10	58	(solvent:DMSO-d ₆) 1.21(3H,t,J = 7.3Hz), 2.58(3H,s), 2.65(2H,q,J = 7.3Hz), 3.60(2H,s), 3.79(2H,d,J = 5.6Hz), 5.46(2H,s) 6.63(1H,s), 7.09(1H,s), 7.70(1H,s), 7.75-7.85(1H,m), 8.1-8.4(3H,m), 12.04(1H,bs), 12.56(1H,s)	
15	54	(solvent:CDCl ₃) 1.31(3H,t,J = 7.6Hz), 1.52(2H,d,J = 6.9Hz), 2.57(3H,s), 2.74(2H,q,J = 7.6Hz), 3.71(2H,s), 4.60(1H,dq,J = 7.6Hz,J = 7.9Hz), 5.49(2H,s), 6.84(1H,s), 7.01(1H,d,J = 7.3Hz), 7.51(1H,s), 7.63(1H,d,J = 7.6Hz), 7.75(1H,dd,J = 7.6Hz,J = 8.2Hz), 7.93(1H,dd,J = 7.6Hz,J = 7.6Hz), 8.22(1H,d,J = 7.9Hz), 8.33(1H,d,J = 8.3Hz)	
20	55	(solvent:CDCl ₃) 1.27(3H,t,J = 7.6Hz), 1.43(2H,d,J = 7.3Hz), 2.59(3H,s), 2.71(2H,q,J = 7.3Hz), 3.72(3H,s), 3.74(2H,s), 4.61(2H,dq,J = 6.9Hz,J = 7.2Hz), 5.39(2H,s), 6.49(1H,s), 7.06(1H,d,J = 7.6Hz), 7.51(1H,s), 7.72(1H,d,J = 7.6Hz), 7.76(1H,dd,J = 7.2Hz,J = 3.4Hz), 8.00(1H,dd,J = 7.6Hz,J = 7.9Hz), 8.27(1H,d,J = 7.9Hz), 8.34(1H,d,J = 8.6Hz)	

25

30

35

40

45

50

55

Table 74

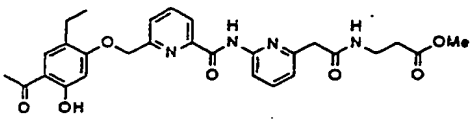
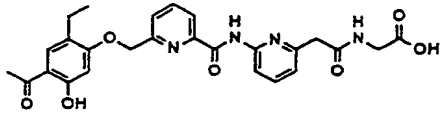
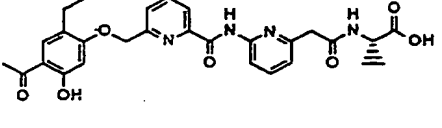
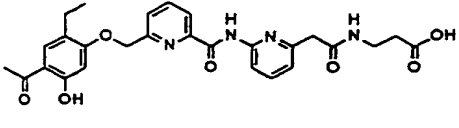
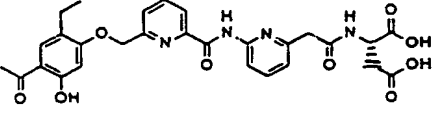
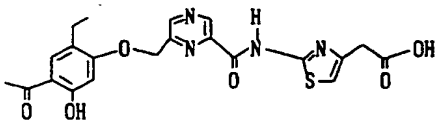
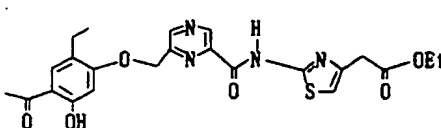
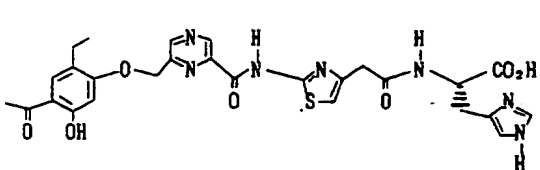
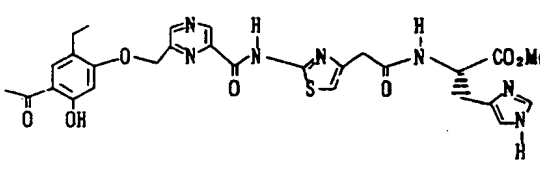
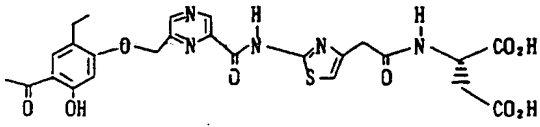
Ex. No.	Structural formula
5 6	
5 7	
5 8	
5 9	
6 0	

Table 75

	¹ H-NMR	δppm
56	(solvent: CDCl ₃) 1.28(3H,t, J = 7.4Hz), 2.59(3H,s), 2.54(2H,t, J = 6.1Hz), 2.70(2H,t, J = 7.4Hz), 3.55(3H,s), 3.56(2H,dd, J = 5.9Hz, J = 6.3Hz), 3.69(2H,s), 5.39(2H,s), 6.50(1H,d, J = 7.6Hz), 7.06(1H,d, J = 7.6Hz), 7.51(1H,s), 7.73(1H,dd, J = 7.9Hz, J = 1.0Hz), 7.75(1H,dd, J = 7.6Hz, J = 7.9Hz), 7.99(1H,dd, J = 7.6Hz, J = 7.9Hz), 8.30(1H,d, J = 7.9Hz, J = 1.0Hz), 8.32(1H,d, J = 8.3Hz)	
57	(solvent: CDCl ₃) 1.28(3H,t, J = 7.6Hz), 2.60(3H,s), 2.72(2H,q, J = 7.5Hz), 3.76(2H,s), 5.40(2H,s), 6.55(1H,s), 7.13(1H,d, J = 7.3Hz), 7.54(1H,s), 7.76(1H,dd, J = 7.3Hz, J = 7.6Hz), 7.81(1H,d, J = 7.6Hz), 8.02(1H,dd, J = 7.9Hz, J = 7.9Hz), 8.25(1H,d, J = 7.3Hz), 8.31(1H,d, J = 8.2Hz)	
58	(solvent: CDCl ₃) 1.31(3H,t, J = 7.6Hz), 1.52(2H,d, J = 6.9Hz), 2.57(3H,s), 2.74(2H,q, J = 7.6Hz), 3.71(2H,s), 4.60(1H,d, J = 7.6Hz, J = 7.9Hz), 5.49(2H,s), 6.84(1H,s), 7.01(1H,d, J = 7.3Hz), 7.51(1H,s), 7.63(1H,d, J = 7.6Hz), 7.75(1H,dd, J = 7.6Hz, J = 8.2Hz), 7.93(1H,dd, J = 7.6Hz, J = 7.6Hz), 8.22(1H,d, J = 7.9Hz), 8.33(1H,d, J = 8.3Hz)	
59	(solvent: CDCl ₃) 1.28(3H,t, J = 7.6Hz), 2.58(3H,s), 2.60(2H,q, J = 5.9Hz), 2.71(2H,q, J = 7.9Hz), 3.70(2H,s), 3.60(2H,q, J = 5.7Hz), 5.44(1H,s), 6.74(1H,s), 7.03(1H,d, J = 7.6Hz), 7.50(1H,s), 7.73(1H,d, J = 7.3Hz), 7.74(1H,dd, J = 8.5Hz, J = 7.3Hz), 8.00(1H,dd, J = 7.9Hz, J = 7.6Hz), 8.25(1H,d, J = 7.6Hz), 8.31(1H,d, J = 8.2Hz)	
60	(solvent: CDCl ₃) 1.29(3H,t, J = 7.6Hz), 2.60(3H,s), 2.73(2H,q, J = 7.5Hz), 2.85(1H,dd, J = 17.2Hz, J = 5.3Hz), 3.00(1H,dd, J = 14.2Hz, J = 4.6Hz), 3.76(2H,s), 4.78(1H,t, J = 5.0Hz), 5.41(2H,s), 6.55(1H,s), 7.13(1H,d, J = 7.6Hz), 7.55(1H,s), 7.74(1H,d, J = 7.8Hz), 7.79(1H,dd, J = 7.6Hz, J = 8.2Hz), 8.02(1H,dd, J = 7.6Hz, J = 7.9Hz), 8.23(1H,d, J = 6.9Hz), 8.30(1H,d, J = 8.6Hz)	

Table 76

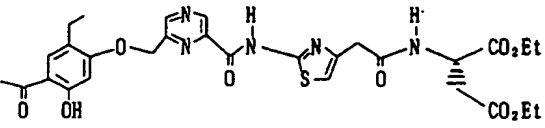
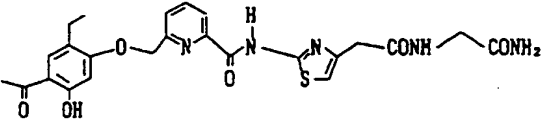
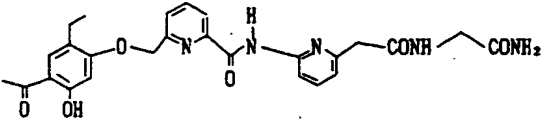
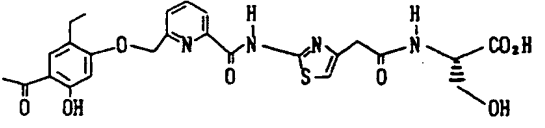
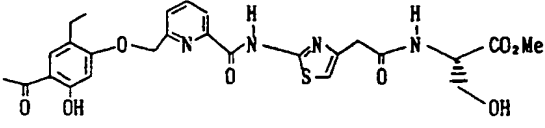
Ex. No.	Structural formula
6 1	
6 2	
6 3	
6 4	
6 5	

EP 0 516 069 A1

Table 77

	¹ H-NMR	δppm
5	61	(solvent:DMSO-d ₆) 1.19(3H,t,J = 7.6Hz), 2.59(3H,s), 2.64(2H,q,J = 7.6Hz), 3.67(2H,s), 5.49(2H,s), 6.69(1H,s), 7.12(1H,s), 7.71 (1H,s), 9.04(1H,s), 9.27(1H,s), 10.06(1H,s), 12.58(1H,br)
10	62	(solvent:CDCl ₃) 1.26(3H,t,J = 7.6Hz), 1.30(3H,t,J = 7.3Hz), 2.60 (3H,s), 2.69(2H,q,J = 7.6Hz), 3.76(2H,d,J = 0.7Hz), 4.22(2H,q,J = 7.3Hz), 5.33(2H,s), 6.47(1H,s), 6.94(1H,s), 7.53(1H,s), 9.08 (1H,s), 9.48(1H,s), 10.90(1H, br), 12.70(1H,s)
15	63	(solvent:DMSO-d ₆) 1.19(3H,t,J = 7.6Hz), 2.59(3H,s), 2.66(2H,q,J = 7.6Hz), 2.89(1H,dd,J = 8.3Hz,15.0Hz), 3.00(1H,dd,J = 5.3Hz,15.0 Hz), 3.58(2H,s), 4.4-4.5(1H,m), 5.49(2H,s), 6.68(1H,s), 6.94 (1H,s), 7.00(1H,s), 7.71(1H,s), 7.87(1H,s), 8.33(1H,d,J = 7.6 Hz), 9.05(1H,s), 9.27(1H,s), 12.60(1H,br)
20	64	(solvent:CDCl ₃) 1.20(3H,t,J = 7.3Hz), 2.60(3H,s), 2.70(2H,q,J = 7.3Hz), 3.1-3.2(2H,m), 3.72(3H,s), 3.75(2H,s), 4.8-4.9(1H,m), 5.36(2H,s), 6.48(1H,s), 6.79(1H,s), 6.91(1H,s), 7.53(1H,s), 7.56(1H,s), 9.10(1H,s), 9.48(1H,s), 12.78(1H,br)
	65	(solvent:DMSO-d ₆) 1.19(3H,t,J = 7.6Hz), 2.59(3H,s), 2.6-2.7(4H, m),3.61(2H,s), 4.5-4.6(1H,m), 5.49(2H,s), 6.69(1H,s), 7.08(1H, s), 8.35(1H,d,J = 7.6Hz), 9.05(1H,s), 9.27(1H,s), 12.60(1H,s),

Table 78

Ex. No.	Structural formula
6 6	
6 7	
6 8	
6 9	
7 0	

EP 0 516 069 A1

Table 79

	¹ H-NMR	δppm
5	66	(solvent:CDCl ₃) 1.16(3H,t,J = 7.6Hz), 1.25(3H,t,J = 7.6Hz), 1.26 (3H,t,J = 7.6Hz), 2.59(3H,s), 2.69(2H,q,J = 7.6Hz), 2.8-3.1(2H,m), 3.71(2H,s), 4.11(2H,q,J = 7.6Hz), 4.21(2H,q,J = 7.6Hz), 4.8-4.9 (1H,m), 5.37(2H,s), 6.47(1H,s), 6.91(1H,s), 7.52(1H,s), 8.03 (1H,s), 9.08(1H,s), 9.49(1H,s), 12.68(1H,s),
10	67	(solvent:CDCl ₃) 1.27(3H,t,J = 7.6Hz), 2.59(3H,t), 2.70(2H,q,J = 7.6Hz), 3.76(2H,s), 3.78(2H,d,J = 0.7Hz), 5.28(2H,s), 6.43(1H, s), 7.51(1H,s), 6.90(1H,s), 7.72(1H,dd,J = 7.9, 1.0Hz), 8.00(1H, dd,J = 7.9, 7.6Hz), 8.25(1H,d,J = 7.9Hz)
15	68	(solvent:CDCl ₃) 1.28(3H,t,J = 7.4Hz), 2.58(3H,s), 2.72(2H,q,J = 7.5Hz), 3.77(2H,s), 4.05(2H,d,J = 5.0Hz), 5.46(2H,s), 6.89(1H, s), 7.03(1H,d,J = 6.6Hz), 7.5(1H,s), 7.72(1H,d,J = 7.9Hz), 7.76 (1H,dd,J = 7.6, 7.9Hz), 7.99(1H,dd,J = 7.6, 7.9Hz), 8.24(1H,d,J = 7.6Hz), 8.30(1H,d,J = 8.3Hz)
20	69	(solvent:CDCl ₃) 1.27(3H,t,J = 7.6Hz), 2.59(3H,s), 2.70(2H,q,J = 7.3Hz), 3.72(2H,s), 3.8-4.0(2H,m), 4.58(3H,t,J = 3.8Hz), 5.33 (2H,s), 6.48(1H,s), 6.94(1H,s), 7.52(1H,s), 7.76(1H,d,J = 7.6 Hz), 8.03(1H,dd,J = 7.9, 7.9Hz), 8.25(1H,d,J = 7.9Hz)
25	70	(solvent:CDCl ₃) 1.27(3H,t,J = 7.4Hz), 2.60(3H,s), 2.71(2H,q,J = 7.5Hz), 3.37(2H,s), 3.73(3H,s), 3.87(1H,dd,J = 11.5, 3.3Hz), 3.97 (1H,dd,11.5, 3.3Hz), 4.6-4.7(1H,m), 5.34(2H,s), 6.48(1H, s), 6.96(1H,s), 7.54(1H,s), 7.77(1H,d,J = 7.6Hz), 8.04(1H,dd,J = 7.9, 7.9Hz), 8.25(1H,d,J = 7.6Hz)

Table 80

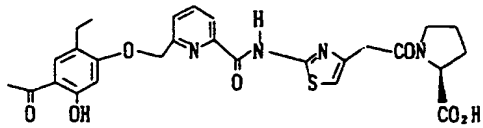
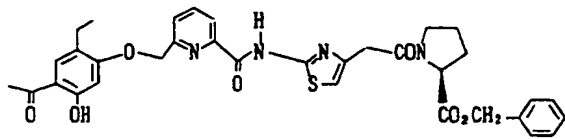
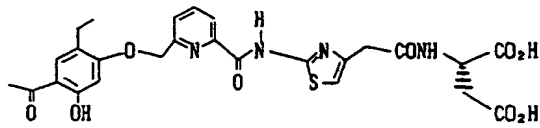
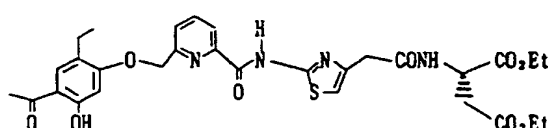
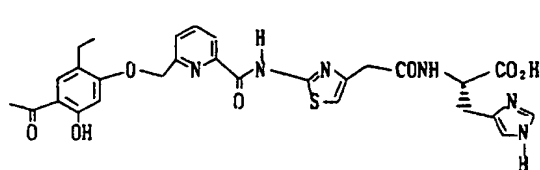
Ex. No.	Structural formula
7 1	
7 2	
7 3	
7 4	
7 5	

Table 81

	¹ H-NMR	δppm
71	(solvent:CDCl ₃) 1.27(3H,t,J = 7.6Hz), 1.5-2.2(4H,m), 2.59(3H,s), 2.70(2H,q,J = 7.6Hz), 3.5-3.7(2H,m), 3.85(2H,d,J = 2.3Hz), 4.6-4.7 (1H,m), 5.32(2H,s), 6.49(1H,s), 6.92(1H,s), 7.51(1H,s), 7.73 (1H,d,J = 7.9Hz), 7.99(1H,dd,J = 7.9, 7.9Hz), 8.23(1H,d,J = 7.9Hz)	
72	(solvent:CDCl ₃) 1.26(3H,t,J = 7.6Hz), 1.9-2.3(4H,m), 2.59(3H,s), 2.70(2H,q,J = 7.5Hz), 3.6-3.8(2H,m), 3.82(2H,s), 4.12(2H,q,J = 7.2Hz), 4.63(1H,dd,J = 8.3, 3.6Hz), 5.18(2H,d,J = 7.9Hz), 5.27(2H, s), 6.44(1H,s), 6.94(1H,s), 7.35(5H,m), 7.51(1H,s), 7.72(1H,d, J = 6.9Hz), 8.00(1H,dd,J = 7.9, 7.9Hz), 8.25(1H,d,J = 7.9Hz)	
73	(solvent:CDCl ₃) 1.27(3H,t,J = 7.6Hz), 2.60(3H,s), 2.71(2H,q,J = 7.3Hz), 2.8-3.1(2H,m), 3.37(2H,d,J = 5.0Hz), 3.71(2H,s), 4.80 (1H,t,J = 4.8Hz), 5.35(2H,s), 6.49(1H,s), 6.93(1H,s), 7.54(1H, s), 7.76(1H,d,J = 7.9Hz), 8.03(1H,dd,J = 7.9, 7.9Hz), 8.23(1H,d,J = 7.9Hz)	
74	(solvent:CDCl ₃) 1.19(3H,t,J = 7.1Hz), 1.24(3H,t,J = 7.4Hz), 1.27 (3H,t,J = 7.8Hz), 2.59(3H,s), 2.70(2H,q,J = 7.2Hz), 2.85(1H,dd,J = 17.2, 4.6Hz), 3.02(1H,dd,J = 16.8, 4.6Hz), 3.72(2H,s), 4.10(2H, q,J = 7.2Hz), 4.20(2H,q,J = 7.1Hz), 4.85(1H,td, J = 4.9, 7.6Hz), 5.31(2H,s), 6.44(1H,s), 6.89(1H,s), 7.51(1H,s), 7.74(1H,d,J = 7.6Hz), 8.01(1H,dd,J = 7.6, 7.9Hz), 8.26(1H,d,J = 7.6Hz)	
75	(solvent:CDCl ₃) 1.27(3H,t,J = 7.5Hz), 2.59(3H,s), 2.69(2H,q,J = 7.3Hz), 3.26(2H,d,J = 5.0Hz), 3.70(2H,s), 4.70(1H,t,J = 5.0Hz), 5.33(2H,s), 6.48(1H,s), 6.95(1H,s), 7.05(1H,s), 7.50(1H,s), 7.76(1H,d,J = 8.0Hz), 8.00(1H,dd,J = 8.0, 8.0Hz), 8.22(1H,d,J = 8.0 Hz)	

Table 82

Ex. No.	Structural formula
76	 <chem>CC(=O)c1cc(O)cc(OCc2ccncc2C(=O)Nc3ccsc3CC(=O)N[C@H](C)Cc4c[nH]cn4)c1</chem>
77	 <chem>CC(=O)c1cc(O)cc(OCc2ccncc2C(=O)Nc3ccsc3CC(=O)N[C@H](C)Cc4c[nH]cn4)c1</chem>
78	 <chem>CC(=O)c1cc(O)cc(OCc2ccncc2C(=O)Nc3ccsc3CC(=O)N[C@H](C)Cc4c[nH]cn4)c1</chem>
79	 <chem>CC(=O)c1cc(O)cc(OCc2ccncc2C(=O)Nc3ccsc3CC(=O)N[C@H](C)c4c[nH]cn4)c1</chem>
80	 <chem>CC(=O)c1cc(O)cc(OCc2ccncc2C(=O)Nc3ccsc3CC(=O)N[C@H](C)c4c[nH]cn4)c1</chem>

EP 0 516 069 A1

Table 83

		¹ H-NMR	δppm
5	76	(solvent:CDCl ₃) 1.26(3H,t,J = 7.5Hz), 2.59(3H,s), 2.69(2H,q,J = 7.5Hz), 3.15(2H,t,J = 4.2Hz), 3.71(3H,s), 3.73(2H,s), 4.84(1H, dt, J = 7.3, 4.2Hz), 5.31(2H,s), 6.45(1H,s), 6.78(1H,s), 6.88(1H, s), 7.50(1H,s), 7.59(1H,s), 7.72(1H,d,J = 7.6Hz), 8.01(1H,dd,J = 7.9, 7.9Hz), 8.26(1H,d,J = 7.6Hz),	
10	77	(solvent:CDCl ₃) 1.27(3H,t,J = 7.5Hz), 1.9-2.5(4H,m), 2.0-2.5(4H, m), 2.60(3H,s), 2.71(2H,q,J = 7.5Hz), 3.70(2H,s), 4.56(1H,t,J = 4.0Hz), 5.35(2H,s), 6.49(1H,s), 6.94(1H,s), 7.36(1H,s), 7.77 (1H,d,J = 7.9Hz), 8.04(1H,dd,J = 7.6, 7.9Hz), 8.24(1H,d,J = 7.6Hz)	
15	78	(solvent:CDCl ₃) 1.21(3H,t,J = 7.1Hz), 1.26(3H,t,J = 7.4Hz), 1.29 (3H,t,J = 7.6Hz), 1.9-2.4(4H,m), 2.59(3H,s), 2.70(2H,q,J = 7.4Hz), 3.70(2H,s), 4.09(2H,q,J = 7.2Hz), 4.19(2H,q,J = 6.9Hz), 4.63(1H, td,J = 3.7, 7.6Hz), 5.33(2H,s), 6.47(1H,s), 6.88(1H,s), 7.51(1H, s), 7.75(1H,d,J = 6.9Hz), 8.02(1H,dd,J = 6.9, 7.6Hz), 8.26(1H,d,J = 6.9Hz)	
20	79	(solvent:CDCl ₃) 1.21(3H,t,J = 7.6Hz), 2.51(3H,s), 2.62(2H,q,J = 7.6Hz), 3.20(2H,br), 4.71(1H,t,J = 5.3Hz), 5.23(2H,s), 6.43(1H, s), 7.41(1H,s), 7.05(1H,s), 7.05(1H,d,J = 7.3Hz), 7.31(1H,s), 7.61(1H,dd,J = 7.9Hz), 7.67(1H,dd,J = 7.9, 7.9Hz), 7.90(1H,dd,J = 7.6, 7.6Hz), 8.12(1H,d,J = 7.3Hz), 8.19(1H,d,J = 8.3Hz),	
25	80	(solvent:CDCl ₃) 1.27(3H,t,J = 7.4Hz), 2.59(3H,s), 2.70(2H,q,J = 7.4Hz), 3.17(2H,d,J = 5.0Hz), 3.67(3H,s), 3.77(2H,s), 4.82(1H, dt,J = 6.9, 5.0 Hz), 5.22(2H,s), 6.35(1H,s), 6.71(1H,s), 7.07 (1H,d,J = 7.3Hz), 7.45(1H,s), 7.51(1H,s), 7.67(1H,d,J = 7.3Hz), 7.76(1H,dd,J = 7.9, 7.9Hz), 7.98(1H,dd,J = 7.9, 7.9Hz), 8.26(1H,d, J = 6.9Hz), 8.32(1H,d,J = 7.9Hz)	

Table 84

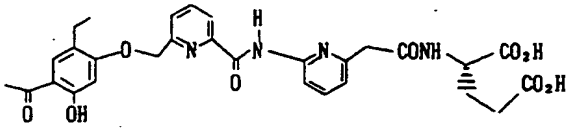
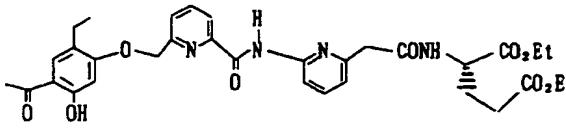
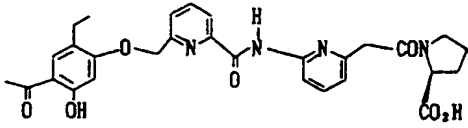
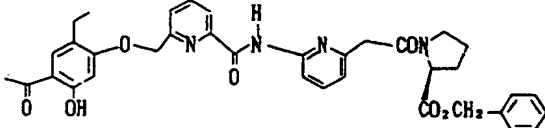
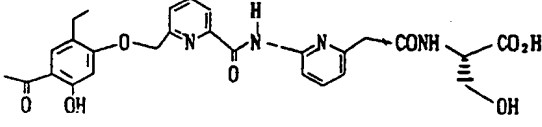
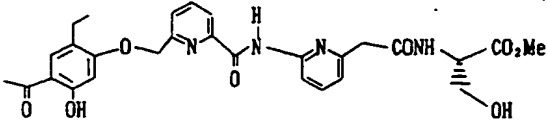
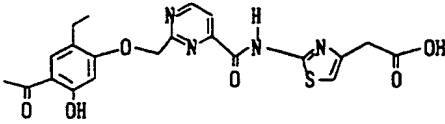
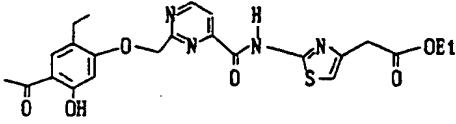
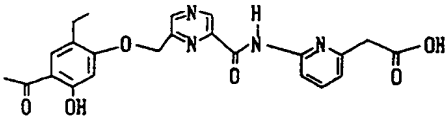
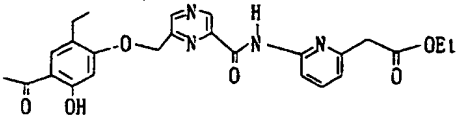
Ex. No.	Structural formula
8 1	
8 2	
8 3	
8 4	
8 5	

Table 85

	¹ H-NMR	δppm
81	(solvent:CDCl ₃) 1.28(3H,t,J = 7.4Hz), 1.9-2.5(4H,m), 2.60(3H,s), 2.72(2H,q,J = 7.4Hz), 3.84(2H,s), 4.5-4.6(1H,m), 5.42(2H,s), 6.56(2H,s), 7.26(1H,d,J = 7.9Hz), 7.54(1H,s), 7.76(1H,d,J = 8.3 Hz), 7.94(1H,dd,J = 7.9, 7.9Hz), 8.03(1H,dd,J = 7.9, 7.6Hz), 8.24 (1H,d,J = 7.9Hz), 8.39(1H,d,J = 8.6Hz)	
82	(solvent:CDCl ₃) 1.16(3H,t,J = 7.3Hz), 1.20(3H,t,J = 7.1Hz), 1.27 (3H,t,J = 7.4Hz), 2.59(3H,s), 2.71(2H,q,J = 7.4Hz), 2.0-2.4(4H,m), 3.74(2H,s), 4.03(2H,q,J = 7.1Hz), 4.1-4.3(2H,m), 4.65(1H,t,d,J = 7.6, 5.3Hz), 5.39(2H,s), 6.49(1H,s), 7.06(1H,d,J = 6.6Hz), 7.51 (1H,s), 7.71(1H,d,J = 7.3Hz), 7.73(1H,dd,J = 7.9, 7.9Hz), 7.99(1H, dd,J = 7.6, 7.9Hz), 8.27(1H,d,J = 7.9Hz), 8.34(1H,d,J = 7.9Hz)	
83	(solvent:CDCl ₃) 1.27(3H,t,J = 7.4Hz), 2.0-2.1(4H,m), 2.58(3H,s), 2.71(2H,q,J = 7.4Hz), 3.67(2H,m), 3.94(2H,d,J = 4.3Hz), 4.75(1H, d,J = 5.9Hz), 5.39(2H,s), 6.56(2H,s), 7.10(1H,d,J = 7.6Hz), 7.50 (1H,s), 7.71(1H,d,J = 7.9Hz), 7.78(1H,dd,J = 7.9, 7.9Hz), 7.98(1H, dd, J = 7.9, 7.6Hz), 8.24(1H,d,J = 7.6Hz), 8.37(1H,d,J = 8.3Hz)	
84	(solvent:CDCl ₃) 1.26(3H,t,J = 7.6Hz), 1.9-2.3(4H,m), 2.58(3H,s), 2.70(2H,q,J = 7.5Hz), 3.6-3.8(2H,m), 3.88(2H,s), 4.12(2H,q,J = 7.2 Hz), 4.63(1H,dd,J = 8.3, 3.6Hz), 5.17(2H,d,J = 7.9Hz), 5.31(2H,s), 6.47(1H,s), 7.15(1H,d,J = 6.6Hz), 7.34(5H,m), 7.50(1H,s), 7.67 (1H,d,J = 7.6Hz), 7.68(1H,dd,J = 7.9, 7.6Hz), 7.97(1H,dd,J = 7.9, 7.6Hz), 8.26(1H,d,J = 6.9Hz), 8.30(1H,d,J = 8.3Hz)	
85	(solvent:CDCl ₃) 1.28(3H,t,J = 7.4Hz), 2.60(3H,s), 2.72(2H,q,J = 7.4Hz), 3.79(2H,s), 3.8-4.1(2H,m), 4.59(1H,t,J = 3.5Hz), 5.39 (2H,s), 6.52(1H,s), 7.54(1H,s), 7.74(1H,d,J = 7.9Hz), 7.80(1H, dd,J = 7.6, 8.3Hz), 8.02(1H,dd,J = 7.9, 7.6Hz), 8.24(1H,d,J = 7.9 Hz), 8.31(1H,d,J = 8.2Hz), 7.15(1H,d,J = 7.3Hz)	

Table 86

Ex. No.	Structural formula
86	
87	
88	
89	
90	

EP 0 516 069 A1

Table 87

	¹ H-NMR	δppm
5	86	(solvent:CDCl ₃) 1.27(3H,t,J = 7.4Hz), 2.58(3H,s), 2.69(2H,q,J = 7.4Hz), 3.74(3H,s), 3.79(2H,s), 4.00(2H,d,J = 3.3Hz), 4.71(1H, dt,J = 7.3, 3.6Hz), 5.38(2H,s), 6.50(1H,s), 7.05(1H,d,J = 6.6Hz), 7.49(1H,s), 7.70(1H,d,J = 7.9Hz), 7.75(1H,dd,J = 7.6, 8.2Hz), 7.98 (1H,dd,J = 7.9, 6.7Hz), 8.25(1H,d,J = 6.6Hz), 8.27(1H,d,J = 8.2Hz)
10	87	(solvent:DMSO-d ₆) 1.19(3H,t,J = 7.6Hz), 2.60(3H,s), 2.64(2H,q,J = 7.6Hz), 3.53(2H,s), 5.49(2H,s), 6.55(1H,s), 6.89(1H,s), 7.64 (1H,s), 8.04(1H,d,J = 5.0Hz), 9.05(1H,s) (DMSO-d ₆)
	88	(solvent:CDCl ₃) 1.27(3H,t,J = 7.6Hz), 1.29(3H,t,J = 7.3Hz), 2.58 (3H,s), 2.71(2H,q,J = 7.6Hz), 3.76(2H,s), 4.21(2H,q,J = 7.3Hz), 5.43(2H,s), 6.41(1H,s), 6.94(1H,s), 7.51(1H,s), 8.13(1H,d,J = 5.0Hz), 9.09(1H,d,J = 5.0Hz), 10.93(br), 12.64(1H,s)
15	89	(solvent:DMSO-d ₆) 1.22(3H,t,J = 7.6Hz), 2.59(2H,s), 2.67(2H,q, J = 7.6Hz), 3.73(2H,s), 5.56(2H,s), 6.71(1H,s), 7.20(1H,d,J = 7.6 Hz), 7.71(1H,s), 7.89(1H,dd,J = 7.6Hz,7.9Hz), 8.16(1H,d,J = 7.9 Hz), 9.08(1H,s), 9.32(1H,s), 10.22(1H,s), 12.58(1H,s)
20	90	(solvent:CDCl ₃) 1.27(3H,t,J = 7.6Hz), 1.28(3H,t,J = 7.3Hz), 2.60 (3H,s), 2.70(2H,q,J = 7.6Hz), 3.80(2H,s), 4.21(2H,q,J = 7.3Hz), 5.38(2H,s), 6.50(1H,s), 7.12(1H,dd,J = 0.7Hz,7.6Hz), 7.52(1H,s), 7.78(1H,t,J = 7.9Hz), 8.34(1H,d,J = 8.3Hz), 9.04(1H,s), 10.06(1H, s), 12.68(1H,s)

25

30

35

40

45

50

55

Table 88

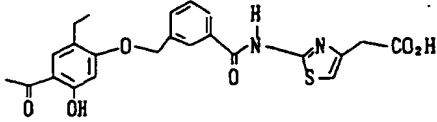
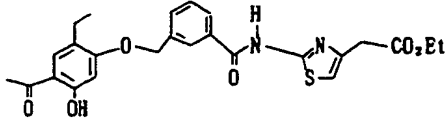
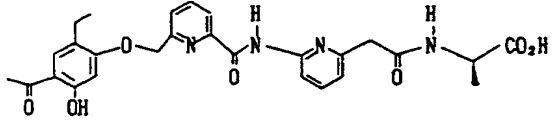
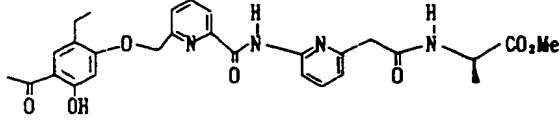
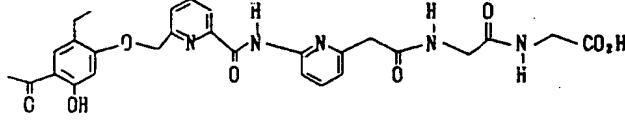
Ex. No.	Structural formula
9 1	
9 2	
9 3	
9 4	
9 5	

Table 89

	¹ H-NMR	δppm
5	91	(solvent:CDCl ₃) 1.22(3H,t,J = 7.6Hz), 2.58(3H,s), 2.65(2H,q,J = 7.6Hz), 3.72(2H,s), 5.20(2H,s), 6.47(1H,s), 6.87(1H,s), 7.50 (1H,s), 7.58(1H,dd,J = 7.6, 7.6Hz), 7.69(1H,d,J = 7.6Hz), 7.98(1H,d,J = 7.6Hz), 8.09(1H,s)
10	92	(solvent:CDCl ₃) 1.22(3H,t,J = 7.4Hz), 1.28(3H,t,J = 7.1Hz), 2.58 (3H,s), 2.64(2H,q,J = 7.4Hz), 3.69(2H,s), 4.19(2H,q,J = 7.1Hz), 5.18(2H,s), 6.45(1H,s), 6.86(1H,s), 7.47(1H,s), 7.57(1H,dd,J = 7.6, 7.6Hz), 7.68(1H,d,J = 7.6Hz), 7.88(1H,d,J = 7.6Hz), 8.02(1H, s)
15	93	(solvent:CDCl ₃) 1.28(3H,t,J = 7.6Hz), 1.47(3H,d,J = 7.3Hz), 2.60 (3H,s), 2.72(2H,q,J = 7.6Hz), 3.89(2H,s), 4.50(1H,dt,J = 7.2, 7.3 Hz), 5.45(2H,s), 6.57(1H,s), 7.34(1H,d,J = 7.6Hz), 7.53(1H,s), 7.78(1H,d,J = 7.9Hz), 8.02(1H,dd,J = 7.6, 7.9Hz), 8.03(1H,dd,J = 7.6, 7.6Hz), 8.23(1H,d,J = 7.6Hz), 8.45(1H,d,J = 8.2Hz),
20	94	(solvent:CDCl ₃) 1.27(3H,t,J = 7.6Hz), 1.43(3H,d,J = 7.3Hz), 2.59 (3H,s), 2.71(2H,q,J = 7.6Hz), 3.72(3H,s), 3.74(2H,s), 4.61(1H, qd,J = 7.1Hz), 5.39(2H,s), 6.49(1H,s), 7.06(1H,d,J = 7.3Hz), 7.51 (1H,s), 7.72(1H,d,J = 7.3Hz), 7.76(1H,dd,J = 7.9, 7.6Hz), 8.00(1H, dd,J = 7.9, 7.6Hz), 8.27(1H,d,J = 8.6Hz), 8.34(1H,d,J = 8.3Hz)
25	95	(solvent:CDCl ₃ /MeoD(4/1)) 1.28(3H,t,J = 7.6Hz), 2.60(3H,s), 2.72(2H,q,J = 7.6Hz), 3.77(2H,s), 3.97(2H,s), 3.99(2H,s), 5.38 (2H,s), 6.53(1H,s), 7.14(1H,d,J = 7.6Hz), 7.37(1H,s), 7.75(1H,d, J = 7.9Hz), 7.79(1H,dd,J = 7.6, 8.2Hz), 8.02(1H,dd,J = 7.6, 7.9Hz), 8.25(1H,d,J = 7.9Hz), 8.30(1H,d,J = 8.2Hz)

Table 90

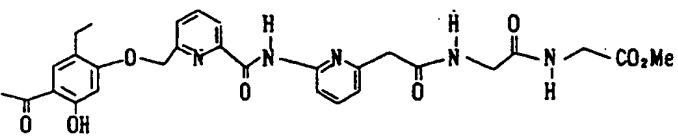
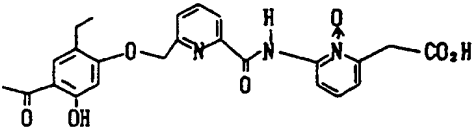
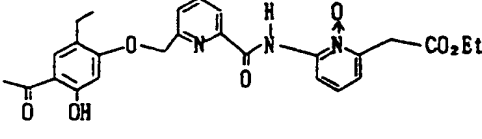
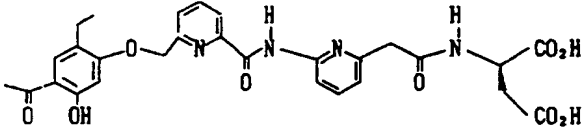
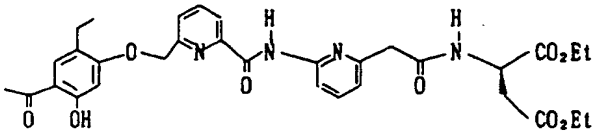
Ex. No.	Structural formula
9 6	
9 7	
9 8	
9 9	
1 0 0	

Table 91

	¹ H-NMR	δppm
96	(solvent:CDCl ₃) 1.21(3H,t,J=7.1Hz), 1.27(3H,t,J=7.4Hz), 2.58(3H,s), 2.71(2H,q,J=7.4Hz), 3.78(2H,s), 4.0-4.1(4H,m), 4.12(2H,q,J=7.1Hz), 5.40(2H,s), 6.52(1H,s), 7.07(1H,d,J=7.3Hz), 7.50(1H,s), 7.72(1H,d,J=7.9Hz), 7.76(1H,t,J=8.3, 7.6Hz), 7.99(1H,dd,J=7.9, 7.9Hz), 8.27(1H,d,J=8.6Hz), 8.30(1H,d,J=8.9Hz)	
97	(solvent:DMSO-d ₆) 1.30(3H,t,J=7.6Hz), 2.59(3H,s), 2.72(2H,q,J=7.6Hz), 3.49(1H,s), 4.13(2H,s), 5.40(2H,s), 6.48(1H,s), 7.17(1H,dd,J=1.8Hz,7.9Hz), 7.51(1H,s), 7.61(1H,dd,J=7.9Hz,8.3Hz), 7.76(1H,d,J=7.9Hz), 8.02(1H,dd,J=7.9Hz, 7.9Hz), 8.26(1H,d,J=8.6 Hz), 8.75(1H,dd,J=1.8Hz,8.3Hz), 12.18(1H,br), 12.63(1H,s).	
98	(solvent:CDCl ₃) 1.27(3H,t,J=7.6Hz), 1.31(1H,t,J=7.1Hz), 2.58(3H,s), 2.70(2H,q,J=7.6Hz), 3.99(2H,s), 4.26(2H,q,J=7.1Hz), 5.35(2H,s), 6.46(1H,s), 7.11(1H,dd,J=1.7Hz,7.9Hz), 7.36(1H,dd, J=7.9Hz,7.9Hz), 7.49(1H,s), 7.72(1H,dd,J=1.0Hz,7.9Hz), 7.98(1H,dd,J=7.9Hz,7.9Hz), 8.23(1H,dd,J=1.0Hz,7.9Hz), 8.63(1H,dd, J=2.0Hz,8.6Hz), 12.29(1H,br), 12.62(1H,s)	
99	(solvent:CDCl ₃) 1.29(3H,t,J=7.4Hz), 2.57(3H,s), 2.72(2H,t,J=7.4Hz), 2.96(1H,dd,J=17.0, 4.5Hz), 3.09(1H,dd,J=17.0, 4.5Hz), 3.77(2H,s), 4.85(1H,br), 5.49(2H,d,J=3.3Hz), 6.72(1H,s), 7.02(1H,d,J=8.3Hz), 7.49(1H,s), 7.65(1H,d,J=7.9Hz), 7.75(1H,dd,J=7.6, 8.3Hz), 7.94(1H,dd,J=7.6, 8.3Hz), 7.94(1H,dd,J=7.9, 7.6 Hz), 8.19(1H,d,J=7.6Hz), 8.32(1H,d,J=8.3Hz)	
100	(solvent:CDCl ₃) 1.10(3H,t,J=7.0Hz), 1.17(3H,t,J=7.1Hz), 1.28(3H,t,J=7.4Hz), 2.59(3H,s), 2.71(2H,q,J=7.4Hz), 2.85(1H,dd,J=17.0, 4.6Hz), 3.02(1H,dd,J=17.0, 4.6Hz), 3.75(2H,s), 4.00(2H, q,J=7.1Hz), 4.16(2H,q,J=7.0Hz), 4.85(1H,qt,J=7.6, 4.6Hz), 5.39(2H,s), 6.49(1H,s), 7.05(1H,d,J=7.3Hz), 7.51(1H,s), 7.72(1H,d, J=7.6Hz), 7.73(1H,dd,J=7.3, 7.6Hz), 7.99(1H,dd,J=7.6, 7.9Hz), 8.27(1H,d,J=7.3Hz), 8.34(1H,d,J=8.3Hz)	

Table 92

Ex. No.	Structural formula
1 0 1	
1 0 2	
1 0 3	
1 0 4	
1 0 5	

Table 93

	¹ H-NMR	δppm
101	(solvent:DMSO-d ₆) 1.17(3H,t,J = 7.6Hz), 2.56(3H,s), 2.59(1H,m), 2.69(1H,m), 3.59(2H,s), 3.6-4.3(2H,br), 4.56(1H,m), 5.29(2H, s), 6.60(1H,s), 6.96(1H,s), 7.56(1H,t,J = 7.9Hz), 7.64(1H,s), 7.68(1H,d,J = 7.9Hz), 8.07(1H,d,J = 7.9Hz), 8.19(1H,s), 8.23(1H,d,J = 7.6Hz), 12.6(1H,s)	
102	(solvent:CDCl ₃ /DMSO-d ₆ (10/1)) 1.15-1.31(9H,m), 2.57(3H,s), 2.64(2H,q,J = 7.3Hz), 2.84(1H,dd,J = 17.2, 4.6Hz), 3.03(1H,dd,J = 17.2, 4.3Hz), 3.67(2H,s), 4.15-4.27(4H,m), 4.85(1H,ddd,J = 7.9, 4.6, 4.3Hz), 5.19(1H,s), 6.46(1H,s), 6.78(1H,s), 7.48(1H,s), 7.57(1H,t,J = 7.9Hz), 7.69(1H,d,J = 7.9Hz), 7.94(1H,brd,J = 8.3Hz), 7.97(1H,d,J = 7.9Hz), 8.10(1H,s), 12.68(1H,s)	
103	(solvent:DMSO-d ₆) 1.21(3H,t,J = 7.3Hz), 2.58(H,s), 2.6-2.7(4H, m), 4.08(1H,s), 4.60(1H,m), 5.46(2H,s), 5.6-6.4(2H,br), 6.62 (1H,s), 7.68(1H,s), 7.80(2H,d), 8.15(2H,m), 8.78(1H,d,J = 7.9 Hz), 12.55(1H,s)	
104	(solvent:CDCl ₃) 1.23-1.65(9H,m), 2.59(3H,s), 2.70(2H,q,J = 7.3 Hz), 2.85(1H,dd,J = 17.2, 4.6Hz), 3.05(1H,dd,J = 17.2, 4.6Hz), 4.10(2H,s), 4.15(2H,q,J = 7.3Hz), 4.22(2H,q,J = 7.3Hz), 4.87(1H, dt,J = 7.9, 4.6Hz), 5.32(1H,s), 6.45(1H,s), 7.24(1H,brd), 7.52 (1H,s), 7.75(1H,d,J = 7.3Hz), 8.01(1H,t,J = 7.9Hz), 8.26(1H,d,J = 7.9Hz), 12.67 (1H,s)	
105	(solvent:DMSO-d ₆) 0.96(6H,m), 1.30(3H,t,J = 7.6Hz), 2.17(1H,m), 2.58(3H,s), 2.73(2H,q,J = 7.6Hz), 3.75(2H,m), 4.67(1H,m), 5.42 (2H,s), 6.83(1H,s), 7.02(1H,d,J = 7.9Hz), 7.51(1H,s), 7.65(1H,d, J = 7.9Hz), 7.75(1H,t,J = 7.9Hz), 7.95(1H,t,J = 7.9Hz), 8.22(1H,d,J = 7.9Hz), 8.32(1H,d,J = 7.9Hz), 8.91(1H,brd), 10.87(1H,s)	

Table 94

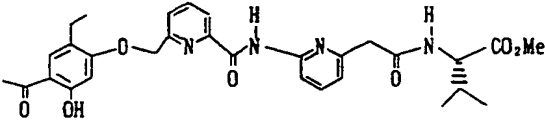
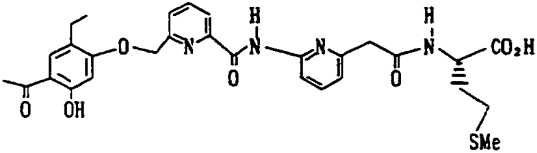
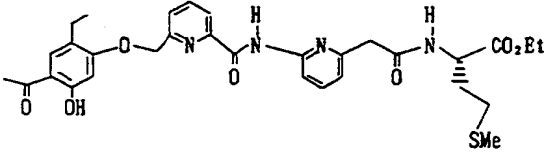
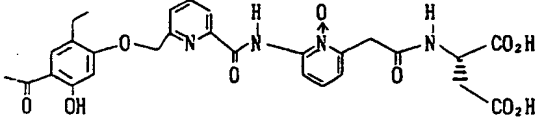
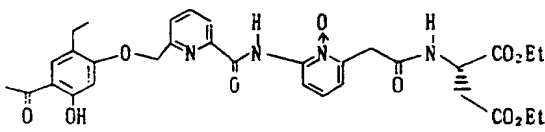
Ex. No.	Structural formula
1 0 6	
1 0 7	
1 0 8	
1 0 9	
1 1 0	

Table 95

	¹ H-NMR	δppm
106	(solvent:CDCl ₃) 0.91(3H,m), 1.27(3H,t,J = 7.3Hz), 2.18(1H,m), 2.59(3H,s), 2.71(2H,q,J = 7.3Hz), 3.71(3H,s), 3.76(2H,s), 4.60(1H,s), 5.34(2H,s), 6.46(1H,s), 7.05(1H,d,J = 7.6Hz), 7.51(1H, s), 7.73(1H,t,J = 7.6Hz), 7.78(1H,d,J = 7.9Hz), 7.97(1H,br), 8.00(1H,t,J = 7.9Hz), 8.27(1H,d,J = 7.9Hz), 8.35(1H,d,J = 7.9Hz), 10.54(1H,s), 12.62(1H,s)	
107	(solvent:DMSO-d ₆) 1.31(3H,t,J = 7.6Hz), 2.01(3H,s), 2.15(1H,m), 2.35(1H,m), 2.55(2H,m), 2.58(3H,s), 2.74(2H,q,J = 7.6Hz), 3.80(1H,d,J = 15.8Hz), 3.68(1H,d,J = 15.8Hz), 4.73(1H,m), 5.48(2H,s), 6.83(1H,s), 7.02(1H,d,J = 7.6Hz), 7.51(1H,s), 7.63(1H,d,J = 7.6 Hz), 7.75(1H,t,J = 7.6Hz), 7.94(1H,t,J = 7.6Hz), 8.22(1H,d,J = 7.6 Hz), 8.33(1H,d,J = 7.6Hz), 9.08(1H,brd), 10.87(1H,s)	
108	(solvent:CDCl ₃) 1.1-1.3(6H,m), 2.00(3H,s), 2.05-2.2(2H,m), 2.47(2H,m), 2.59(3H,s), 2.70(2H,q,J = 7.3Hz), 3.74(2H,s), 4.16(2H,m), 4.71(1H,m), 5.40(2H,s), 6.50(1H,s), 7.06(1H,d,J = 7.6 Hz), 7.51(1H,s), 7.75(1H,t,J = 7.6Hz), 7.77(1H,d,J = 7.9Hz), 7.96(1H,br), 8.00(1H,t,J = 7.6Hz), 8.27(1H,d,J = 7.3Hz), 8.34(1H,d,J = 8.3Hz), 10.53(1H,s), 12.63(1H,s)	
109	(solvent:DMSO-d ₆) 1.21(3H,t,J = 7.3Hz), 2.51(3H,s), 2.63(4H,m), 3.89(2H,s), 4.59(1H,m), 5.42(2H,s), 6.63(1H,s), 7.29(1H,d,J = 8.3Hz), 7.44(1H,t,J = 8.3Hz), 7.65(1H,s), 7.83(1H,d,J = 7.3Hz), 8.18(1H,t,J = 7.3Hz), 8.23(1H,brd), 8.47(1H,d,J = 8.3Hz), 8.59(1H, d,J = 7.3Hz), 12.16(1H,s), 12.51(1H,s), 12.6(2H,br)	
110	(solvent:CDCl ₃) 1.15(3H,t,J = 7.3Hz), 1.17(3H,t,J = 7.3Hz), 1.27(3H,t,J = 7.3Hz), 2.59(3H,s), 2.71(1H,q,J = 7.3Hz), 2.83(1H,dd,J = 16.8Hz,5.3Hz), 2.94(1H,dd,J = 16.8Hz,5.3Hz), 3.96(1H,d,J = 13.5 Hz), 4.07(1H,d,J = 13.5 Hz), 4.11(2H,q,J = 7.3Hz), 4.12(2H,q,J = 7.3Hz), 4.81(1H,dt,J = 8.2Hz,5.3Hz), 5.39(2H,s), 6.48(1H,s), 7.18(1H, dd,J = 7.9Hz,1.7Hz), 7.41(1H,t,J = 7.9Hz), 7.50(1H,s), 7.76(1H,d, J = 7.9Hz), 8.01(1H,t,J = 7.9Hz), 8.25(1H,d,J = 7.9Hz), 8.63(1H,dd, J = 7.4Hz,1.7Hz), 8.69(1H,d,J = 8.2Hz), 12.32(1H,s), 12.61(1H,s)	

Table 96

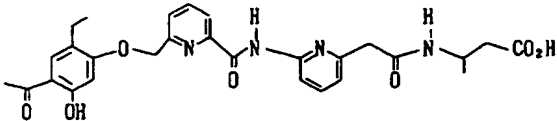
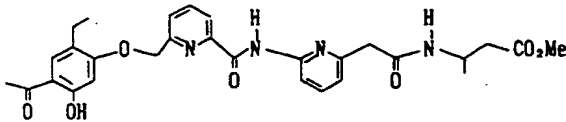
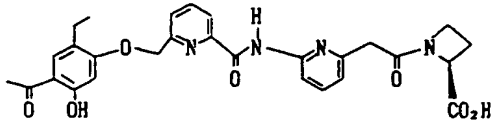
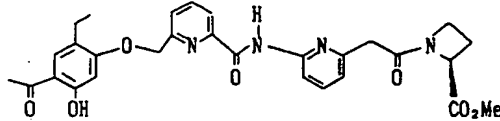
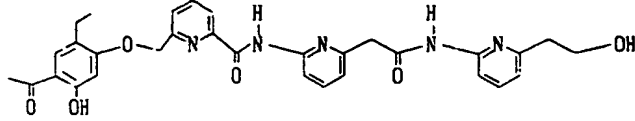
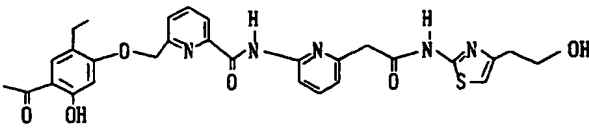
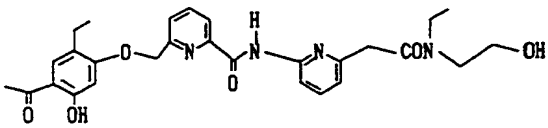
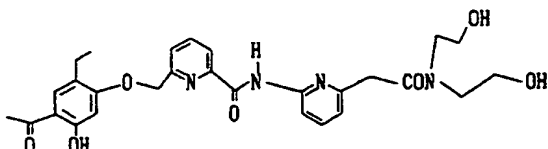
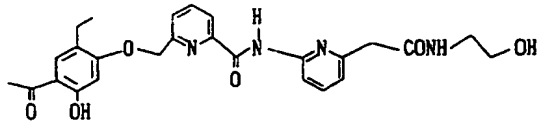
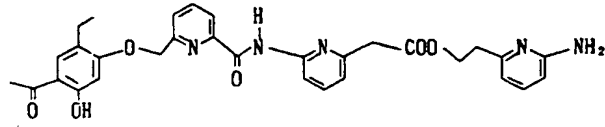
Ex. No.	Structural formula
1 1 1	
1 1 2	
1 1 3	
1 1 4	
1 1 5	

Table 97

	¹ H-NMR	δppm
111	(solvent:DMSO-d ₆) 1.12(3H,d,J = 6.6Hz), 1.22(3H,t,t,J = 7.6Hz), 2.30 (1H,dd,J = 15.2Hz,7.3Hz), 2.46(1H,dd,J = 15.2Hz,7.3Hz), 2.58(3H, s), 2.67(2H,q,J = 7.6Hz), 3.56(2H,s), 4.10(1H,m), 5.47(2H,s), 6.64(2H,s), 7.13(1H,d,J = 7.6Hz), 7.69(1H,s), 7.80-7.86(2H,m), 8.10-8.30(4H,m), 10.35(1H,s), 12.17(1H,s), 12.56(1H,s)	
112	(solvent:CDCl ₃) 1.26(6H,m), 2.53(2H,d,J = 5.3Hz), 2.59(3H,s), 2.71(3H,s), 2.71(2H,m), 3.55(3H,s), 3.68(2H,s), 4.36(1H,m), 5.36(2H,s), 6.47(1H,s), 7.06(1H,d,J = 7.6Hz), 7.42(1H,brd,J = 7.9 Hz), 7.51(1H,s), 7.70(1H,d,J = 7.6Hz), 7.75(1H,t,J = 7.6Hz), 7.99 (1H,t,J = 7.6Hz), 8.27(1H,d,J = 7.6Hz), 8.31(1H,d,J = 7.6Hz), 10.48 (1H,s), 12.65(1H,s)	
113	(solvent:DMSO-d ₆) 1.23(3H,t,J = 7.3Hz), 2.14(1H,m), 2.6(1H,m), 2.58(3H,s), 2.67(2H,q,J = 7.3Hz), 3.45-3.70(2H,m), 3.83(1H,m), 4.22(1H,m), 5.02(0.4H,m), 4.57(0.6H,m), 5.48(2H,s), 6.65(1H, s), 7.14(1H,m), 7.69(1H,s), 7.65-7.90(2H,m), 8.15-8.30(3H,m), 10.32(0.6H,s), 10.34(0.4H,s), 12.55(1H,s), 12.90(1H,br)	
114	(solvent:CDCl ₃) 1.27(3H,t,J = 7.6Hz), 2.20-2.40(1H,m), 2.5-2.7 (1H,m), 2.59(3H,s), 2.71(2H,q,J = 7.6Hz), 3.64(0.4H,s), 3.68(0.6 H,s), 3.77(0.6H,s), 3.80(0.4H,s), 4.05-4.40(2H,m), 4.79(0.6H, m), 4.95(0.4H,m), 5.34(2H,s), 6.48(1H,s), 7.13(0.4H,d,J = 7.6 Hz), 7.19(0.6H,d,J = 7.6Hz), 7.51(1H,s), 7.70(1H,d,J = 7.6Hz), 7.75(1H,m), 7.98(1H,t,J = 7.6Hz), 8.27(1H,d,J = 7.6Hz), 8.32(1H,d, J = 7.6Hz), 10.34(1H,s), 12.67(1H,s)	
115	(solvent:CDCl ₃) 1.28(3H,t,J = 7.6Hz), 2.58(3H,s), 2.72(2H,q,J = 7.6Hz), 2.91(2H,t,t,J = 5.7Hz), 3.87(2H,s), 3.92(2H,t,t,J = 5.7Hz), 5.46(2H,s), 6.60(1H,s), 6.88(1H,d,J = 7.3Hz), 7.12(1H,d,J = 6.6 Hz), 7.50(1H,s), 7.62(1H,dd,J = 7.6, 8.3Hz), 7.73(1H,d,J = 7.9Hz), 7.78(1H,dd,J = 7.6, 8.3Hz), 7.98(1H,dd,J = 7.6 7.9Hz), 8.06(1H,d, J = 8.3Hz), 8.27(1H,d,J = 7.9Hz), 8.40(1H,d,J = 7.6Hz)	

Table 98

Ex. No.	Structural formula
1 1 6	
1 1 7	
1 1 8	
1 1 9	
1 2 0	

EP 0 516 069 A1

Table 99

	¹ H-NMR	δppm
5	116	(solvent:CDCl ₃ /MeODC(1/4))1.28(3H,t,J = 7.6Hz), 2.60(3H,s), 2.72(2H,q,J = 7.6Hz), 2.88(2H,t,J = 6.3Hz), 3.86(2H,t,J = 6.3Hz), 3.97(2H,s), 5.39(2H,s), 6.52(1H,s), 6.68(1H,s), 7.19(1H,d,J = 7.6Hz), 7.55(1H,s), 7.76(1H,d,J = 7.9Hz), 7.83(1H,dd,J = 8.2,7.6Hz), 8.05(1H,dd,J = 7.6,J = 7.9Hz), 8.25(1H,d,J = 7.6Hz), 8.33(1H,d,J = 8.2Hz)
10	117	(solvent:CDCl ₃) 1.0-1.3(5H,m), 2.59(2H,s), 2.71(2H,q,J = 7.5Hz), 3.4-3.9(6H,m), 3.4-3.9(6H,m), 3.93(2H,s), 5.35(2H,s), 6.49(1H,s), 7.0-7.2(1H,m), 7.51(1H,s), 7.6-8.4(5H,m)
	118	(solvent:CDCl ₃) 1.27(3H,t,J = 7.4Hz), 2.58(3H,s), 2.70(2H,q,J = 7.4Hz), 3.6-4.0(8H,m), 4.00(2H,s), 5.35(2H,s), 6.51(1H,s), 7.11(1H,d,J = 7.6Hz), 7.50(1H,s), 7.70(1H,d,J = 7.6Hz), 7.76(1H,dd,J = 7.6,7.6Hz), 7.97(1H,dd,J = 7.6,7.9Hz), 8.24(1H,d,J = 7.9Hz), 8.32(1H,d,J = 7.6Hz)
15	119	(solvent:CDCl ₃) 1.28(3H,t,J = 7.4Hz), 2.60(3H,s), 2.71(2H,q,J = 7.4Hz), 3.42(2H,t,J = 6.6Hz), 3.68(2H,t,J = 6.6Hz), 3.71(2H,s), 5.37(2H,s), 6.50(1H,s), 7.13(1H,d,J = 7.6Hz), 7.53(1H,s), 7.74(1H,d,J = 7.6Hz), 7.76(1H,dd,J = 8.2,7.6Hz), 8.02(1H,dd,J = 7.6,7.6Hz), 8.25(1H,d,J = 7.6Hz), 8.27(1H,d,J = 8.2Hz)
20	120	(solvent:CDCl ₃) 1.27(3H,t,J = 7.4Hz), 2.59(3H,s), 2.71(2H,q,J = 7.4Hz), 2.93(2H,t,J = 6.8Hz), 4.48(2H,t,J = 6.8Hz), 5.32(2H,s), 6.31(1H,d,J = 8.1Hz), 6.45(1H,d,J = 8.1Hz), 7.03(1H,d,J = 7.6Hz), 7.29(1H,d,J = 8.1,8.1Hz), 7.69(1H,d,J = 7.6Hz) 7.71(1H,dd,J = 7.6,7.6Hz), 7.97(1H,dd,J = 7.6,7.6Hz), 8.26(1H,d,J = 7.6Hz), 8.33(1H,d,J = 7.6Hz)

25

30

35

40

45

50

55

Table 100

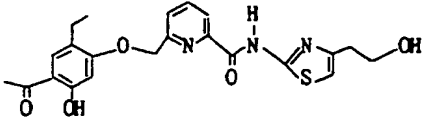
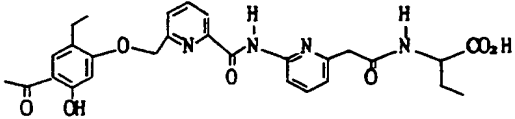
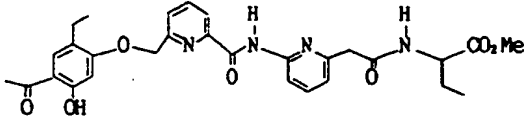
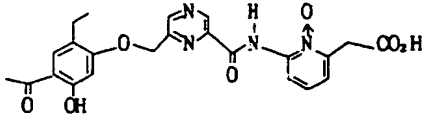
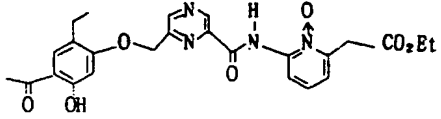
Ex. No.	Structural formula
1 2 1	
1 2 2	
1 2 3	
1 2 4	
1 2 5	

Table 101

	¹ H-NMR	δppm
121	(solvent:CDCl ₃) 1.28(3H,t,J = 7.4Hz), 2.59(3H,s), 2.71(2H,q,J = 7.4Hz), 2.96(2H,t,J = 5.5Hz), 3.96(2H,t,J = 5.5Hz), 5.33(2H,s), 6.45(1H,s), 6.73(1H,s), 7.51(1H,s), 7.72(1H,d,J = 6.9Hz), 8.00(1H,dd,J = 7.9,7.6Hz), 8.25(1H,dd,J = 7.6Hz)	
122	(solvent:DMSO-d ₆) 0.41(3H,t,J = 7.6Hz), 1.30(3H,t,J = 7.6Hz), 1.7-1.9(2H,m), 2.57(3H,s), 3.74(2H,ABq,J = 15.4Hz,5.5Hz), 4.66(1H,m), 5.46(2H,s), 6.83(1H,s), 7.02(1H,d,J = 7.6Hz), 7.51(1H,s), 7.63(1H,d,J = 7.6Hz), 7.75(1H,t,J = 7.6Hz), 7.94(1H,t,J = 7.6Hz), 8.22(1H,d,J = 7.6Hz), 8.32(1H,d,J = 7.6Hz), 8.94(1H,m), 10.86(1H,s)	
123	(solvent:CDCl ₃) 0.88(3H,t,J = 7.3Hz), 1.27(3H,t,J = 7.6Hz), 1.7-1.9(2H,m), 2.59(3H,s), 2.71(2H,q,J = 7.6Hz), 3.71(3H,s), 3.74(2H,s), 4.63(1H,m), 5.37(2H,s), 6.47(1H,s), 7.06(1H,d,J = 7.6Hz), 7.71(1H,d,J = 7.6Hz), 7.75(1H,t,J = 7.6Hz), 7.86(1H,m), 8.00(1H,t,J = 7.6Hz), 8.27(1H,d,J = 7.6Hz), 8.35(1H,m,J = 7.6Hz), 10.53(1H,s), 12.63(1H,s)	
124	(solvent:DMSO-d ₆) 1.19(3H,t,J = 7.6Hz), 2.59(3H,s), 2.65(2H,q,J = 7.6Hz), 3.89(2H,s), 5.53(2H,s), 6.73(1H,s), 7.37(1H,d,J = 7.9Hz), 7.51(1H,t,J = 7.9Hz), 7.69(1H,s), 8.46(1H,d,J = 7.9Hz), 9.13(1H,s), 9.37(1H,s), 11.96(1H,s), 12.50(1H,br), 12.54(1H,s)	
125	(solvent:CDCl ₃) 1.26(3H,t,J = 7.6Hz), 1.31(3H,t,J = 7.3Hz), 2.60(3H,s), 2.69(2H,q,J = 7.6Hz), 3.98(3H,s), 4.25(2H,q,J = 7.3Hz), 5.39(2H,s), 6.47(1H,s), 7.15(1H,dd,J = 8.3Hz, 2.0Hz), 7.39(1H,t,J = 8.3Hz), 7.52(1H,s), 8.61(1H,dd,J = 8.3Hz,2.0Hz), 9.07(1H,s), 9.46(1H,s), 12.12(1H,s), 12.65(1H,s)	

Table 102

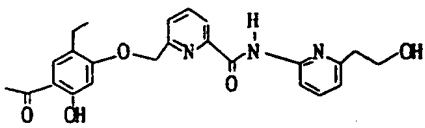
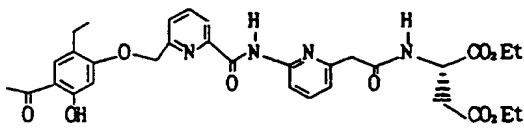
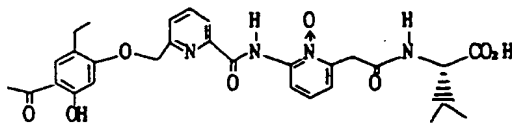
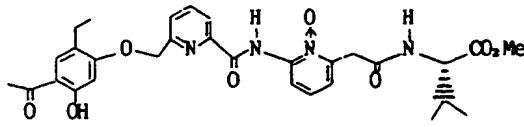
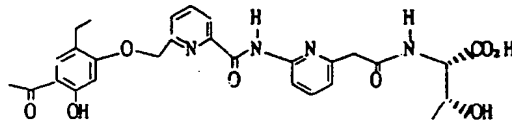
Ex. No.	Structural formula
1 2 6	
1 2 7	
1 2 8	
1 2 9	
1 3 C	

Table 103

	¹ H-NMR	δppm
126	(solvent:CDCl ₃) 1.28(3H,t,J = 7.4Hz), 2.71(2H,q,J = 7.4Hz), 3.02(2H,t,J = 5.5Hz), 4.05(2H,t,J = 5.5Hz), 5.34(2H,s), 6.49(1H,s), 6.98(1H,d,J = 7.6Hz), 7.50(1H,s), 7.70(1H,d,J = 7.9Hz), 7.72(1H,dd,J = 7.9,7.9Hz), 7.98(1H,d,J = 7.9,7.6Hz), 8.27(1H,d,J = 7.6Hz), 8.30(1H,d,J = 8.2Hz)	
127	(solvent:CDCl ₃) 1.10(3H,t,J = 7.1Hz), 1.17(3H,t,J = 7.3Hz), 1.27(3H,t,J = 8.1Hz), 2.59(3H,s), 2.71(2H,q,J = 7.2Hz), 2.84(1H,dd,J = 16.8,4.6Hz), 3.02(1H,dd,J = 16.8,4.3Hz), 3.75(2H,s), 4.00(2H,q,J = 7.1Hz), 4.16(2H,q,J = 7.0Hz), 4.85(1H,dt,J = 7.9,4.6Hz), 5.39(2H,s), 6.49(1H,s), 7.05(1H,dd,J = 7.6,0.6Hz), 7.51(1H,s), 7.72(1H,d,J = 7.6Hz), 7.75(1H,dd,J = 7.9,7.9Hz), 7.99(1H,dd,J = 7.6,7.9Hz), 8.28(1H,dd,J = 8.6,1.0Hz), 8.34(1H,dd,J = 8.2,0.7Hz)	
128	(solvent:DMSO-d ₆) 0.90(3H,d,J = 7.6Hz), 0.91(3H,d,J = 7.6Hz), 1.19(3H,t,J = 7.3Hz), 2.07(1H,m), 2.58(3H,s), 2.65(2H,q,J = 7.3Hz), 3.92(2H,ABq,J = 21.8,15.5Hz), 4.18(1H,dd,J = 8.3,5.6Hz), 5.42(2H,s), 6.62(1H,s), 7.29(1H,dd,J = 8.3,2.0Hz), 7.48(1H,t,J = 8.3Hz), 7.68(1H,s), 7.85(1H,m), 8.20(2H,m), 8.45(1H,dd,J = 8.3,2.0Hz), 8.46(1H,d,J = 8.3Hz), 12.17(1H,s), 12.51(1H,s), 12.60(1H,s)	
129	(solvent:CDCl ₃) 0.88(3H,t,J = 7.3Hz), 0.89(3H,t,J = 7.3Hz), 1.27(3H,t,J = 7.6Hz), 2.18(1H,m), 2.59(3H,s), 2.71(2H,q,J = 7.6Hz), 3.65(3H,s), 4.04(2H,ABq,J = 17.5,13.2Hz), 4.40(1H,m), 5.36(2H,s), 6.45(1H,s), 7.18(1H,dd,J = 8.3,2.0Hz), 7.41(1H,t,J = 8.3Hz), 7.51(1H,s), 7.74(1H,d,J = 7.9Hz), 8.00(1H,t,J = 7.9Hz), 8.25(1H,d,J = 7.9Hz), 8.63(1H,dd,J = 8.3,2.0Hz), 8.76(1H,d,J = 8.6Hz), 12.38(1H,s), 12.62(1H,s)	
130	(solvent:DMSO-d ₆) 1.10(3H,d,J = 7.3Hz), 1.22(3H,t,J = 7.6Hz), 2.58(3H,s), 2.67(2H,q,J = 7.6Hz), 3.76(2H,ABq,J = 20.5,14.9Hz), 4.17(1H,br), 4.26(1H,m), 4.95(1H,m), 5.47(2H,s), 6.63(1H,s), 7.20(1H,d,J = 7.6Hz), 7.69(1H,s), 7.82(2H,m), 8.18(4H,m), 10.36(1H,s), 12.50(1H,br), 12.55(1H,s)	

Table 104

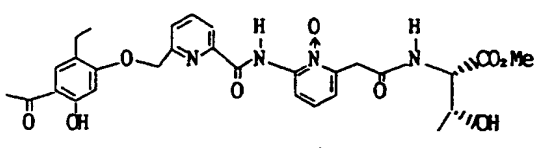
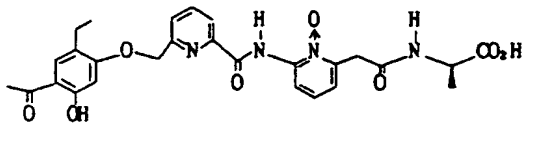
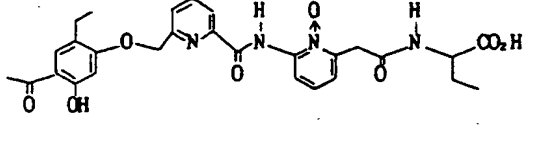
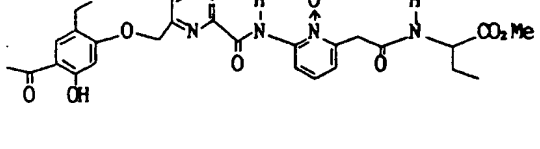
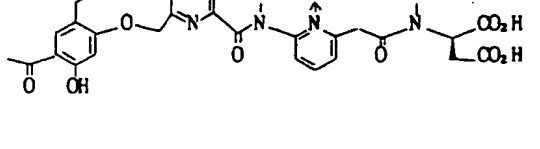
Ex. No.	Structural formula
1 3 1	
1 3 2	
1 3 3	
1 3 4	
1 3 5	

Table 105

	¹ H-NMR	δppm
131	(solvent:CDCl ₃) 1.16(3H,d,J = 7.3Hz), 1.26(3H,t,J = 7.6Hz), 2.69(2H,q,J = 7.6Hz), 3.01(1H,br), 3.69(3H,s), 4.05(2H,ABq,J = 20.1Hz,13.9Hz), 4.50(1H,m), 4.54(1H,m), 5.36(2H,s), 6.49(1H,s), 7.20(1H,dd,J = 8.3Hz, 1.7Hz), 7.41(1H,t,J = 8.3Hz), 7.48(1H,s), 7.72(1H,d,J = 7.9Hz), 7.98(1H,t,J = 7.9Hz), 8.21(1H,d,J = 7.9Hz), 8.51(1H,d,J = 8.6Hz), 8.60(1H,dd,J = 8.3,1.7Hz), 12.34(1H,s), 12.64(1H,s)	
132	(solvent:DMSO-d ₆) 1.19(3H,t,J = 7.3Hz), 1.31(3H,d,J = 7.3Hz), 2.58(3H,s), 2.64(2H,q,J = 7.6Hz), 3.85(2H,m), 4.24(1H,m), 5.43(2H,s), 6.63(1H,s), 7.31(1H,dd,J = 8.3,1.7Hz), 7.47(1H,t,J = 8.3Hz), 7.68(1H,s), 7.85(1H,m), 8.21(2H,m), 8.46(1H,dd,J = 8.3,1.7Hz), 8.54(1H,d,J = 7.9Hz), 12.15(1H,s), 12.50(1H,s), 12.55(1H,br)	
133	(solvent:DMSO-d ₆) 0.92(3H,t,J = 7.6Hz), 1.20(3H,t,J = 7.6Hz), 1.6-1.9(1H,m), 2.58(3H,s), 2.65(2H,q,J = 7.6Hz), 3.89(2H,ABq,J = 20.8,15.8Hz), 4.17(1H,m), 5.42(2H,s), 6.63(1H,s), 7.30(1H,dd,J = 8.3Hz,2.0Hz), 7.47(1H,t,J = 8.3Hz), 7.68(1H,s), 7.85(2H,m), 8.21(2H,m), 8.45(1H,dd,J = 8.3,2.0Hz), 8.50(1H,d,J = 7.9Hz), 12.16(1H,s), 12.50(1H,s), 12.55(1H,br)	
134	(solvent:CDCl ₃) 0.89(3H,t,J = 7.3Hz), 1.27(3H,t,J = 7.6Hz), 1.70-1.85(2H,m), 2.59(3H,s), 2.71(2H,q,J = 7.6Hz), 3.69(3H,s), 4.02(2H,ABq,J = 18.8,13.2Hz), 4.45(1H,m), 5.38(2H,s), 6.48(1H,s), 7.18(1H,dd,J = 7.9,2.0Hz), 7.41(1H,t,J = 7.9Hz), 7.50(1H,s), 7.75(1H,d,J = 7.9Hz), 8.00(1H,t,J = 7.9Hz), 8.25(1H,d,J = 7.9Hz), 8.61(1H,brd), 8.63(1H,dd,J = 7.9Hz,2.0Hz), 12.33(1H,s), 12.63(1H,s)	
135	(solvent:DMSO-d ₆) 1.20(3H,t,J = 7.6Hz), 2.58(3H,s), 2.65(2H,q,J = 7.6Hz), 2.7-2.9(2H,m), 3.87(2H,s), 4.58(1H,m), 5.43(2H,s), 6.64(1H,s), 7.30(1H,dd,J = 8.3,2.0Hz), 7.47(1H,t,J = 8.3Hz), 7.68(1H,s), 7.84(1H,m), 8.21(1H,m), 8.46(1H,dd,J = 8.3Hz,2.0Hz), 8.61(1H,d,J = 7.9Hz), 12.14(1H,s), 12.51(1H,s), 12.55(2H,br)	

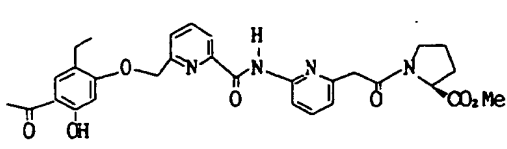
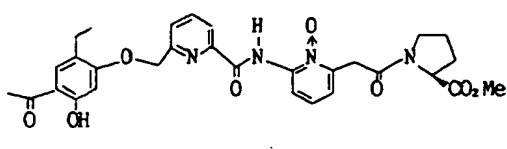
Table 106

Ex. No.	Structural formula
1 3 6	
1 3 7	
1 3 8	
1 3 9	
1 4 0	

Table 107

	¹ H-NMR	δppm
136	(solvent:CDCl ₃) 1.15(3H,t,J = 7.3Hz), 1.17(3H,t,J = 7.3Hz), 1.27(3H,t,J = 7.6Hz), 2.59(3H,s), 2.71(2H,q,J = 7.6Hz), 2.80-2.95(2H,m), 3.93-4.16(6H,m), 4.81(1H,m), 5.39(2H,s), 6.47(1H,s), 7.18(1H,d,J = 8.3Hz), 7.41(1H,t,J = 8.3Hz), 7.51(1H,s), 7.76(1H,d,J = 7.9Hz), 8.01(1H,t,J = 7.9Hz), 8.25(1H,d,J = 7.9Hz), 8.62(1H,dd,J = 8.3,1.7Hz), 8.69(1H,d,J = 7.9Hz), 12.31(1H,s), 12.61(1H,s)	
137	(solvent:DMSO-d ₆) 1.09(3H,d,J = 7.6Hz), 1.20(3H,t,J = 7.6Hz), 2.58(3H,s), 2.66(2H,q,J = 7.6Hz), 3.96(2H,ABq,J = 20.8,15.8Hz), 4.10(1H,br), 4.24(1H,m), 4.90(1H,m), 5.42(2H,s), 6.63(1H,s), 7.31(1H,dd,J = 7.9,2.0Hz), 7.48(1H,t,J = 7.9Hz), 7.68(1H,s), 7.85(1H,m), 8.17-8.30(3H,m), 12.16(1H,s), 12.50(1H,s), 12.55(1H,br)	
138	(solvent:CDCl ₃) 1.18(2H,d,J = 6.6Hz), 1.27(3H,t,J = 7.6Hz), 2.58(3H,s), 2.69(2H,q,J = 7.6Hz), 3.72(3H,s), 3.80(2H,s), 4.34(4H,m), 4.61(1H,m), 5.37(2H,s), 6.49(1H,s), 7.06(1H,d,J = 7.9Hz), 7.49(1H,s), 7.70(1H,d,J = 7.9Hz), 7.76(1H,t,J = 7.9Hz), 7.97(1H,t,J = 7.9Hz), 8.25(1H,d,J = 7.9Hz), 8.29(1H,d,J = 7.9Hz), 8.46(1H,brd,J = 8.3Hz), 10.57(1H,s), 12.70(1H,s)	
139	(solvent:CDCl ₃) 1.27(3H,t,J = 7.6Hz), 1.41(3H,d,J = 7.3Hz), 2.59(3H,s), 2.71(2H,q,J = 7.6Hz), 3.66(3H,s), 4.01(2H,ABq,J = 29.7Hz,13.2Hz), 4.51(1H,m), 5.40(2H,s), 6.50(1H,s), 7.18(1H,dd,J = 8.3,2.0Hz), 7.41(1H,t,J = 8.3Hz), 7.50(1H,s), 7.75(1H,d,J = 7.9Hz), 8.00(1H,t,J = 7.9Hz), 8.26(1H,d,J = 7.9Hz), 8.52(1H,d,J = 7.6Hz), 8.64(1H,dd,J = 8.3,2.0Hz), 12.31(1H,s), 12.63(1H,s)	
140	(solvent:DMSO-d ₆) 1.20(3H,t,J = 7.6Hz), 1.90-2.52(4H,m), 2.58(3H,s), 2.66(2H,q,J = 7.6Hz), 3.70(2H,m), 3.99(2H,ABq,J = 29.7,16.2Hz), 4.29(1H,m), 5.24(2H,s), 6.63(1H,s), 7.33(1H,dd,J = 7.6,2.0Hz), 7.47(1H,t,J = 8.3Hz), 7.68(1H,s), 7.85(1H,dd,J = 5.6,3.3Hz), 8.20(2H,s), 8.46(1H,dd,J = 8.3,2.0Hz), 12.14(1H,s), 12.51(1H,s)	

Table 108

Ex. No.	Structural formula
1 4 1	
1 4 2	

EP 0 516 069 A1

Table 109

	¹ H-NMR	δppm
5	141	(solvent:CDCl ₃) 1.27(3H,t,J = 7.6Hz), 1.9-2.3(4H,m), 2.59(3H,s), 2.71(2H,q,J = 7.6Hz), 3.73(3H,s), 3.6-3.9(2H,m), 3.87(2H,m), 4.55(1H,m), 5.33(2H,s), 6.47(1H,s), 7.18(1H,d,J = 7.9Hz), 7.51(1H,s), 7.69(1H,d,J = 7.9Hz), 7.74(1H,t,J = 7.9Hz), 7.98(1H,t,J = 7.9Hz), 8.27(1H,d,J = 7.9Hz), 8.31(1H,d,J = 7.9Hz), 10.34(1H,s), 12.67(1H,s)
10	142	(solvent:CDCl ₃) 1.27(3H,t,J = 7.6Hz), 1.9-2.3(4H,m), 2.58(3H,s), 2.70(2H,q,J = 7.6Hz), 3.74(3H,s), 3.7-3.9(2H,m), 3.90(1H,d,J = 15.8Hz), 4.26(1H,d,J = 15.8Hz), 4.61(1H,m), 5.35(2H,s), 6.46(1H,s), 7.25(1H,brd), 7.37(1H,t,J = 7.9Hz), 7.50(1H,s), 7.73(1H,d,J = 7.9Hz), 7.98(1H,t,J = 7.9Hz), 8.24(1H,d,J = 7.9Hz), 8.59(1H,d,J = 7.9Hz), 12.29(1H,s), 12.65(1H,s)
15		

20

25

30

35

40

45

50

55

Table 110

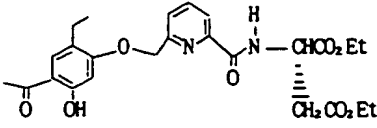
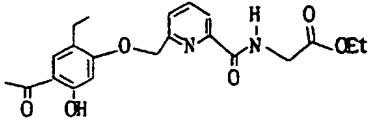
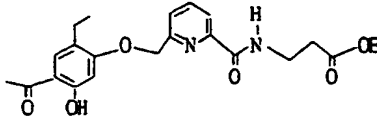
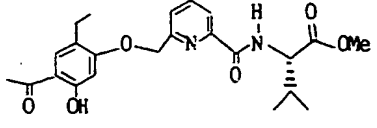
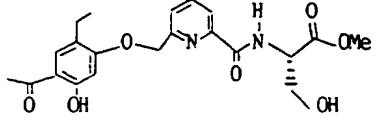
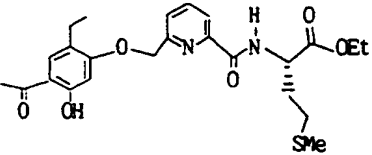
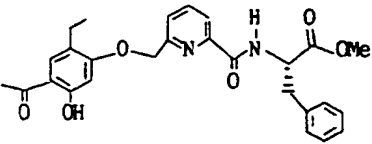
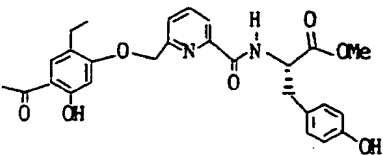
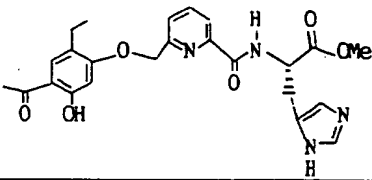
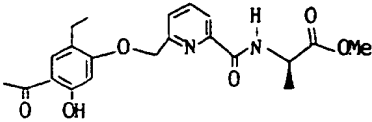
Ex. No.	Structural formula
1 4 3	
1 4 4	
1 4 5	
1 4 6	
1 4 7	

Table 111

	¹ H-NMR	δppm
143	(solvent: CDCl ₃) 1.26(3H,t,J = 7.4Hz), 1.27(3H,t,J = 7.4Hz), 1.30(3H,t,J = 7.0Hz), 2.58(3H,t), 2.69(2H,q,J = 7.4Hz), 2.97(1H,dd,J = 16.8,4.6Hz), 3.13(1H,dd,J = 16.8,4.0Hz), 4.19(2H,qd,J = 7.3,3.0Hz), 4.27(2H,q,J = 7.3, 3.0Hz), 5.06(1H,td,J = 8.3,5.0Hz), 5.27(1H,s), 6.46(1H,s), 7.49(1H,s), 7.64(1H,dd,J = 7.6,1.0Hz), 7.91(1H,dd,J = 7.6,7.6Hz), 8.14(1H,dd,J = 7.6,1.0Hz)	
144	(solvent: CDCl ₃) 1.26(3H,t,J = 7.6Hz), 1.32(3H,t,J = 7.3Hz), 2.58(3H,s), 2.68(2H,q,J = 7.6Hz), 4.2-4.3(4H,m), 5.26(2H,s), 6.45(1H,s), 7.49(1H,s), 7.64(1H,d,J = 7.6Hz), 7.92(1H,dd,J = 6.9,7.6Hz), 8.15(1H,d,J = 6.9Hz), 12.66(1H,s)	
145	(solvent: CDCl ₃) 1.25(3H,t,J = 7.6Hz), 1.28(3H,t,J = 7.3Hz), 2.6-2.7(4H,m), 3.7-3.8(2H,m), 4.1-4.2(2H,q,J = 7.3Hz), 5.24(2H,s), 6.45(1H,s), 7.49(1H,s), 7.61(1H,d,J = 7.9Hz), 7.90(1H,dd,J = 6.6,7.9Hz), 8.14(1H,d,J = 6.6Hz), 8.42(1H,br), 12.66(1H,s)	
146	(solvent: CDCl ₃) 1.02(6H,dd,J = 4.0Hz,6.9Hz), 1.26(3H,t,J = 7.6Hz), 2.2-2.4(1H,m), 2.58(3H,s), 2.69(2H,q,J = 7.6Hz), 3.78(3H,s), 4.75(1H,dd,J = 5.3,9.2Hz), 5.29(2H,s), 6.49(1H,s), 7.50(1H,s), 7.64(1H,d,J = 7.9Hz), 7.91(1H,dd,J = 7.9,7.9Hz), 8.15(1H,d,J = 7.9Hz), 8.44(1H,d,J = 9.2Hz), 12.66(1H,s)	
147	(solvent: CDCl ₃) 1.25(3H,t,J = 7.6Hz), 2.58(3H,s), 2.68(2H,q,J = 7.6Hz), 3.85(3H,s), 4.0-4.2(2H,m), 4.8-4.9(1H,m), 5.29(2H,s), 6.51(1H,s), 7.49(1H,s), 7.65(1H,d,J = 7.6Hz), 7.92(1H,dd,J = 7.6,7.9Hz), 8.15(1H,d,J = 7.9Hz), 8.80(1H,d,J = 7.9Hz), 12.70(1H,s)	

Table 112

Ex. No.	Structural formula
1 4 8	
1 4 9	
1 5 0	
1 5 1	
1 5 2	

EP 0 516 069 A1

Table 113

	¹ H-NMR	δppm
5	148	(solvent:CDCl ₃) 1.26(3H,t,J = 7.6Hz), 1.32(3H,t,J = 7.3Hz), 2.0-2.2(1H,m), 2.12(3H,s), 2.3-2.4(1H,m), 2.5-2.7(4H,m), 2.58(3H,s), 4.26(2H,q,J = 7.3Hz), 4.8-5.0(1H,m), 5.29(2H,s), 6.47(1H,s), 7.50(1H,s), 7.64(1H,dd,J = 1.0,7.6Hz), 7.91(1H,dd,J = 7.6,7.6Hz), 8.14(1H,dd,J = 1.0Hz,7.6Hz), 8.52(1H,d,J = 8.6Hz), 12.66(1H,s)
10	149	(solvent:CDCl ₃) 1.25(3H,t,J = 7.6Hz), 2.58(3H,s), 2.67(2H,q,J = 7.6Hz), 3.26(2H,dd,J = 1.8Hz,6.3Hz), 3.75(3H,s), 5.07(1H,dt,J = 8.3,6.3Hz), 5.22(2H,s), 6.45(1H,s), 7.1-7.4(5H,m), 7.50(1H,s), 7.62(1H,d,J = 7.3Hz), 7.89(1H,dd,J = 6.9Hz,7.3Hz), 8.11(1H,d,J = 6.9Hz), 8.41(1H,d,J = 8.3Hz), 12.67(1H,s)
15	150	(solvent:CDCl ₃) 1.25(3H,t,J = 7.6Hz), 2.58(3H,s), 2.68(2H,q,J = 7.6Hz), 3.1-3.2(2H,m), 3.76(3H,s), 5.02(1H,dt,J = 8.6Hz,5.9Hz), 5.21(2H,d,J = 2.0Hz), 6.09(1H,s), 6.42(1H,s), 6.76(1H,dd,J = 2.3Hz,8.9Hz), 7.02(1H,d,J = 8.9Hz), 7.50(1H,s), 7.61(1H,d,J = 7.6Hz), 7.88(1H,dd,J = 7.5Hz,7.6Hz), 8.10(1H,d,J = 7.5Hz), 8.40(1H,d,J = 8.6Hz), 12.63(1H,s)
20	151	(solvent:CDCl ₃) 1.25(3H,t,J = 7.6Hz), 2.58(3H,s), 2.68(2H,q,J = 7.6Hz), 3.30(2H,d,J = 5.6Hz), 3.79(3H,s), 5.0-5.1(1H,m), 5.27(2H,d,J = 4.62Hz), 6.42(1H,s), 6.86(1H,d,J = 1.3Hz), 7.49(1H,s), 7.6-7.7(2H,m), 7.89(1H,dd,J = 7.6Hz,7.6Hz), 8.12(1H,dd,J = 1.0Hz,7.9Hz), 8.8-8.9(1H,m), 12.80(1H,s)
25	152	(solvent:CDCl ₃) 1.26(3H,t,J = 7.6Hz), 1.57(3H,d,J = 6.9Hz), 2.58(3H,s), 2.69(2H,q,J = 7.6Hz), 3.80(3H,s), 4.82(1H,dq,J = 6.9Hz,8.3Hz), 5.28(2H,s), 6.47(1H,s), 7.50(1H,s), 7.63(1H,dd,J = 1.0Hz,7.9Hz), 7.91(1H,dd,J = 7.9Hz,7.9Hz), 8.14(1H,dd,J = 1.0,7.9Hz), 8.43(1H,d,J = 8.3Hz), 12.66(1H,s)

30

35

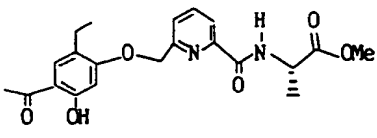
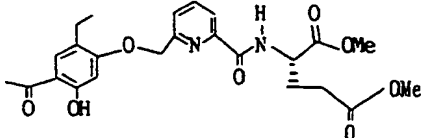
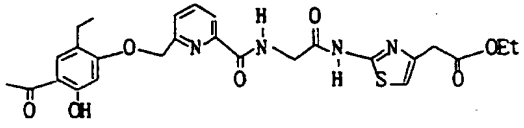
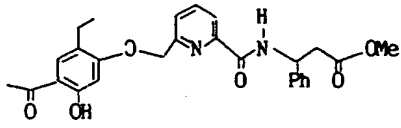
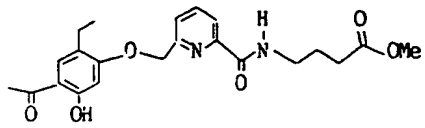
40

45

50

55

Table 114

Ex. No.	Structural formula
1 5 3	
1 5 4	
1 5 5	
1 5 6	
1 5 7	

EP 0 516 069 A1

Table 115

	¹ H-NMR	δppm
5	153	(solvent:CDCl ₃) 1.26(3H,t,J = 7.6Hz), 1.57(3H,d,J = 7.3Hz), 2.58(3H,s), 2.69(2H,q,J = 7.6Hz), 3.80(3H,s), 4.82(1H,dq,J = 7.3Hz,7.9Hz), 5.28(2H,s), 6.45(1H,s), 7.50(1H,s), 7.63(1H,d,J = 7.6Hz), 7.91(1H,dd,J = 7.6,7.6Hz), 8.14(1H,d,J = 7.6Hz), 8.43(1H,d,J = 7.9Hz), 12.66(1H,s)
10	154	(solvent:CDCl ₃) 1.26(3H,t,J = 7.6Hz), 2.1-2.5(4H,m), 2.58(3H,s), 2.69(2H,q,J = 7.6Hz), 3.66(3H,s), 3.70(3H,s), 4.8-4.9(1H,m), 5.29(2H,s), 6.48(1H,s), 7.50(1H,s), 7.64(1H,dd,J = 1.0Hz,7.6Hz), 7.91(1H,dd,J = 7.6Hz,7.6Hz), 8.13(1H,dd,J = 1.0,7.6Hz), 8.47(1H,d J = 8.6Hz), 12.65(1H,s)
15	155	(solvent:CDCl ₃) 1.25(3H,t,J = 7.3Hz), 1.26(3H,t,J = 7.6Hz), 2.58(3H,s), 2.69(2H,q,J = 7.6Hz), 3.68(2H,d,J = 1.0Hz), 4.17(2H,q,J = 7.3Hz), 4.42(2H,d,J = 6.3Hz), 5.26(2H,s), 6.45(1H,s), 6.82(1H,t,J = 1.0Hz), 7.50(1H,s), 7.69(1H,d,J = 7.9Hz), 7.96(1H,dd,J = 7.9Hz,8.9Hz), 8.63(1H,br), 9.80(1H,br), 12.67(1H,s)
20	156	(solvent:CDCl ₃) 1.25(3H,t,J = 7.6Hz), 2.58(3H,s), 2.68(2H,q,J = 7.6Hz), 2.97(1H,dd,J = 6.3Hz,15.8Hz), 3.09(1H,dd,J = 6.6,15.8Hz), 3.64(3H,s), 5.27(2H,s), 5.64(1H,ddd,J = 6.3Hz,6.6Hz,8.9Hz), 6.49(1H,s), 7.2-7.5(5H,m), 7.49(1H,s), 7.63(1H,d,J = 7.3Hz), 7.90(1H,dd,J = 7.3Hz,7.3Hz), 8.15(1H,d,J = 7.3Hz), 8.80(1H,d,J = 8.9Hz), 12.66(1H,s)
25	157	(solvent:CDCl ₃) 1.25(3H,t,J = 7.6Hz), 1.9-2.1(2H,m), 2.45(2H,t,J = 7.6Hz), 2.58(3H,s), 2.68(2H,q,J = 7.6Hz), 3.54(2H,m), 3.68(3H,s), 5.25(2H,s), 6.47(1H,s), 7.50(1H,s), 7.61(1H,d,J = 7.6Hz), 7.90(1H,dd,J = 7.6Hz,7.9Hz), 8.10(1H,br), 8.15(1H,d,J = 7.9Hz)

25

30

35

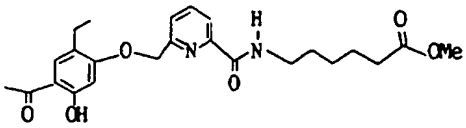
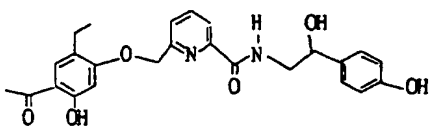
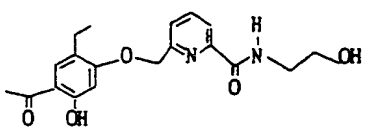
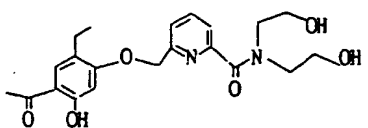
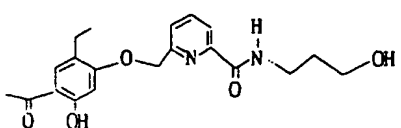
40

45

50

55

Table 116

Ex. No.	Structural formula
1 5 8	
1 5 9	
1 6 0	
1 6 1	
1 6 2	

EP 0 516 069 A1

Table 117

	¹ H-NMR	δppm
5	158	(solvent:CDCl ₃) 1.25(3H,t,J = 7.6Hz), 1.3-1.5(2H,m), 1.6-1.8(4H,m), 2.34(2H,t,J = 7.6Hz), 2.58(3H,s), 2.68(2H,q,J = 7.6Hz), 3.4-3.5(2H,m), 3.67(3H,s), 5.25(2H,s), 6.47(1H,s), 7.49(1H,s), 7.51(1H,d,J = 7.9Hz), 7.90(1H,dd,J = 7.9Hz,7.9Hz), 8.02(1H,br), 8.16(1H,d,J = 7.9Hz), 12.67(1H,s)
10	159	(solvent:DMSO-d ₆) 1.19(3H,t,J = 7.6Hz), 2.52(3H,s), 2.60(2H,q,J = 7.6Hz), 3.5-3.7(2H,m), 4.6-4.8(1H,m), 5.36(2H,s), 5.57(1H,d,J = 4.3Hz), 6.58(1H,s), 6.6-6.7(1H,m), 6.8-6.9(2H,m), 7.1-7.2(1H,m), 7.7-7.8(2H,m), 7.9-8.2(2H,m), 8.5-8.6(1H,m), 9.34(1H,s), 12.56(1H,s)
15	160	(solvent:DMSO-d ₆) 1.25(3H,t,J = 7.6Hz), 2.59(3H,s), 2.67(2H,q,J = 7.6Hz), 2.73(1H,t,J = 5.4Hz), 3.6-3.7(2H,m), 3.8-3.9(2H,m), 5.25(2H,m), 6.49(1H,s), 7.49(1H,s), 7.62(1H,d,J = 7.6Hz), 7.91(1H,dd,J = 7.6Hz,7.6Hz), 8.16(1H,d,J = 7.6Hz), 8.40(1H,br), 12.69(1H,s)
20	161	(solvent:DMSO-d ₆) 1.24(3H,t,J = 7.6Hz), 2.59(3H,s), 2.68(2H,q,J = 7.6Hz), 3.6-4.0(9H,m), 5.25(2H,s), 5.84(1H,t,J = 4.6Hz), 6.43(1H,s), 7.49(1H,s), 7.62(1H,d,J = 7.6Hz), 7.81(1H,d,J = 7.6Hz), 7.95(1H,dd,J = 7.6Hz,7.6Hz), 12.62(1H,s)
	162	(solvent:DMSO-d ₆) 1.25(3H,t,J = 7.6Hz), 1.8-1.9(2H,m), 2.58(3H,s), 2.67(2H,q,J = 7.6Hz), 3.30(1H,t,J = 6.4Hz), 5.25(2H,s), 6.50(1H,s), 7.63(1H,d,J = 7.6Hz), 7.91(1H,dd,J = 7.6Hz,7.6Hz), 8.16(1H,d,J = 7.6Hz), 8.30(1H,br), 12.71(1H,s)

25

30

35

40

45

50

55

Table 118

Ex. No.	Structural formula
1 6 3	 <chem>CC1=CC=C(C=C1)OC2=CC=C(C=C2)OC3=CC=C(C=C3)C(=O)NCCO</chem>
1 6 4	 <chem>CC1=CC=C(C=C1)OC2=CC=C(C=C2)OC3=CC=C(C=C3)C(=O)NCC(=O)OCC</chem>
1 6 5	 <chem>CC1=CC=C(C=C1)OC2=CC=C(C=C2)OC3=CC=C(C=C3)C(=O)N[C@H](C)C(=O)OC</chem>
1 6 6	 <chem>CC1=CC=C(C=C1)OC2=CC=C(C=C2)OC3=CC=C(C=C3)C(=O)N[C@H](C)C(=O)OCC</chem>
1 6 7	 <chem>CC1=CC=C(C=C1)OC2=CC=C(C=C2)OC3=CC=C(C=C3)C(=O)N[C@H](C)C(=O)O</chem>

Table 119

	¹ H-NMR	δppm
5	163	(solvent:DMSO-d ₆) 1.25(3H,t,J = 7.6Hz), 1.32(3H,t,J = 7.1Hz), 2.57(3H,s), 2.68(2H,q,J = 7.6Hz), 3.4-4.0(6H,m), 5.25(2H,s), 6.45(1H,s), 7.49(1H,s), 7.5-7.9(3H,m), 12.61(1H,s)
10	164	(solvent:CDCl ₃) 1.22(3H,t,J = 7.4Hz), 1.32(3H,t,J = 7.1Hz), 2.57(3H,s), 2.63(2H,q,J = 7.4Hz), 4.26(2H,s), 4.27(2H,q,J = 7.1Hz), 5.13(2H,s), 6.44(1H,s), 7.46(1H,s), 7.49(1H,dd,J = 7.6,7.6Hz), 7.59(1H,d,J = 7.6Hz), 7.77(1H,d,J = 7.6Hz), 7.90(1H,s)
15	165	(solvent:CDCl ₃) 1.22(3H,t,J = 7.4Hz), 1.54(2H,d,J = 7.0Hz), 2.57(3H,s), 2.63(2H,q,J = 7.4Hz), 3.80(3H,s), 4.82(1H,q,J = 7.0Hz), 5.14(2H,s), 6.44(1H,s), 7.46(1H,s), 7.48(1H,dd,J = 7.6,7.6Hz), 7.58(1H,q,J = 7.6Hz), 7.76(1H,d,J = 7.6Hz), 7.88(1H,s)
20	166	(solvent:CDCl ₃) 1.22(3H,t,J = 7.6Hz), 1.26(3H,t,J = 7.1Hz), 1.29(3H,t,J = 7.1Hz), 2.57(3H,s), 2.64(2H,q,J = 7.4Hz), 2.97(1H,dd,J = 17.2,4.3Hz), 3.14(1H,dd,J = 17.2,4.3Hz), 4.16(2H,q,J = 7.1Hz), 4.27(2H,q,J = 7.1Hz), 5.04(1H,td,J = 4.3,7.9Hz), 5.15(1H,s), 6.45(1H,s), 7.46(1H,s), 7.49(1H,dd,J = 7.6,7.6Hz), 7.59(1H,d,J = 7.6Hz), 7.77(1H,d,J = 7.6Hz), 7.90(1H,s)
	167	(solvent:CDCl ₃) 1.22(3H,t,J = 7.4Hz), 2.57(3H,s), 2.63(2H,q,J = 7.4Hz), 3.83(3H,s), 4.1-4.2(2H,br), 4.89(1H,dt,J = 7.3,3.6Hz), 5.14(2H,s), 6.44(1H,s), 7.47(1H,s), 7.49(1H dd,J = 7.6,7.6Hz), 7.60(1H,d,J = 7.6Hz), 7.80(1H,d,J = 7.6Hz), 7.91(1H,s)

25

30

35

40

45

50

55

Table 120

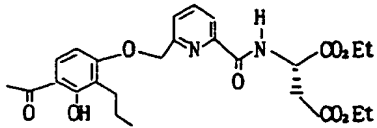
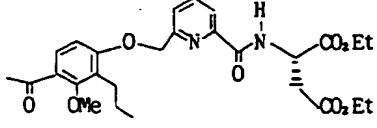
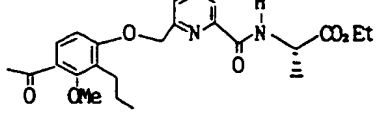
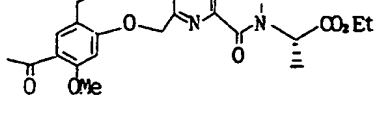
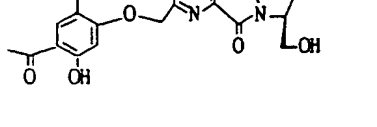
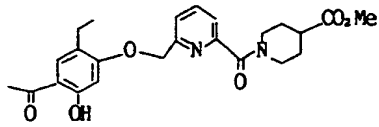
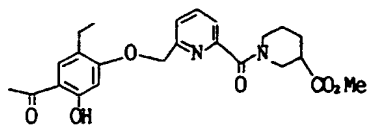
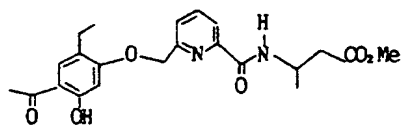
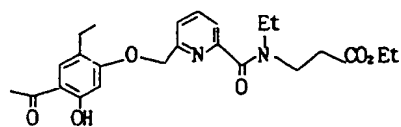
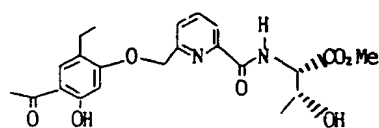
Ex. No.	Structural formula
1 6 8	
1 6 9	
1 7 0	
1 7 1	
1 7 2	

Table 121

	¹ H-NMR	δppm
168	(solvent:CDCl ₃) 0.98(3H,t,J = 7.3Hz), 1.27(3H,t,J = 7.3Hz), 1.30(3H,t,J = 7.1Hz), 1.5-1.7(2H,m), 2.58(3H,s), 2.76(2H,t,J = 7.6Hz), 2.98(1H,dd,J = 16.8,4.9Hz), 3.14(1H,dd,J = 16.8,4.9Hz), 4.1-4.4(4H,m), 5.06(1H,dt,J = 8.6,4.9Hz), 5.32(2H,s), 6.50(1H,d,J = 8.9Hz), 7.61(1H,d,J = 8.9Hz), 7.66(1H,d,J = 8.9Hz), 7.66(1H,d,J = 7.9Hz), 7.91(1H,dd,J = 7.6,7.9Hz), 8.13(1H,d,J = 7.6Hz)	
169	(solvent:CDCl ₃) 1.02(3H,t,J = 7.4Hz), 1.27(3H,t,J = 7.1Hz), 1.30(3H,t,J = 7.1Hz), 1.6-1.7(2H,m), 2.62(3H,t), 2.74(2H,t,J = 7.9Hz), 2.97(1H,dd,J = 17.0,4.9Hz), 3.13(1H,dd,J = 17.0,4.9Hz), 4.1-4.4(4H,m), 5.06(1H,dt,J = 8.3,4.9Hz), 5.29(2H,s), 6.74(1H,d,J = 8.8Hz), 7.57(1H,d,J = 8.8Hz), 7.66(1H,d,J = 7.9Hz), 7.91(1H,dd,J = 7.6,7.9Hz), 8.14(1H,d,J = 7.6Hz)	
170	(solvent:CDCl ₃) 1.02(3H,t,J = 7.3Hz), 1.32(3H,t,J = 7.3Hz), 1.56(3H,d,J = 7.3Hz), 1.6-1.7(2H,m), 2.62(3H,s), 2.75(2H,t,J = 7.9Hz), 3.78(3H,s), 4.26(2H,q,J = 7.2Hz), 4.79(1H,qd,J = 7.8,7.8Hz), 5.29(2H,s), 6.73(1H,d,J = 7.6Hz), 7.57(1H,d,J = 8.6Hz), 7.64(1H,d,J = 7.9Hz), 7.91(1H,dd,J = 7.6,7.9Hz), 8.14(1H,d,J = 7.6Hz)	
171	(solvent:CDCl ₃) 1.24(3H,t,J = 7.2Hz), 1.32(3H,t,J = 7.1Hz), 1.56(3H,d,J = 1.0Hz), 2.58(3H,s), 2.69(2H,q,J = 7.5Hz), 3.88(3H,s), 4.26(2H,q,J = 7.2Hz), 4.81(1H,qd,J = 7.7,7.7Hz), 5.32(2H,s), 6.51(1H,s), 7.72(1H,s), 7.70(1H,d,J = 8.3Hz), 7.93(1H,dd,J = 9.7,7.6Hz), 8.15(1H,d,J = 7.9Hz)	
172	(solvent:CDCl ₃) 1.24(3H,t,J = 7.5Hz), 1.6-2.2(4H,m), 2.57(3H,s), 2.67(2H,q,J = 7.5Hz), 3.5-5.4(7H,m), 6.44-6.46(2H,m), 7.5-8.0(4H,m),	

Table 122

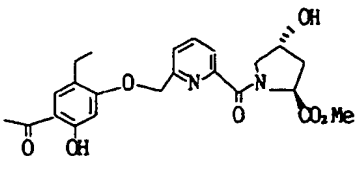
Ex. No.	Structural formula
1 7 3	
1 7 4	
1 7 5	
1 7 6	
1 7 7	

EP 0 516 069 A1

Table 123

	¹ H-NMR	δppm
5	173	(solvent:CDCl ₃) 1.25(3H,t,J = 7.5Hz), 1.7-2.1(5H,m), 2.57(3H,s), 2.67(2H,q,J = 7.5Hz), 3.0-3.3(2H,m), 3.72(3H,s), 3.8-4.0(2H,m), 4.5-4.7(2H,m), 5.24(2H,s), 6.44(1H,s), 7.48(1H,s), 7.53(1H,d,J = 7.6Hz), 7.56(1H,d,J = 7.6Hz), 7.84(1H,dd,J = 7.9,7.9Hz)
10	174	(solvent:CDCl ₃) 1.25(3H,td,J = 7.6,2.0Hz), 1.5-2.0(4H,m), 2.57(3H,s), 2.68(2H,q,J = 7.6Hz), 3.61(1.5H,s), 3.73(1.5H,s), 2.5-5.0(5H,m), 5.24(2H,s), 6.44(1H,s), 7.48(1H,s), 7.5-8.0(3H,m)
15	175	(solvent:CDCl ₃) 1.26(3H,t,J = 7.4Hz), 1.38(2H,d,J = 6.9Hz), 2.58(3H,s), 2.5-2.7(4H,m), 3.72(3H,s), 4.5-4.6(1H,m), 5.27(2H,s), 6.48(1H,s), 7.49(1H,s), 7.61(1H,d,J = 7.9Hz), 7.89(1H,dd,J = 7.9,7.6Hz), 8.15(1H,d,J = 7.6Hz)
20	176	(solvent:CDCl ₃) 1.22(3H,t,J = 6.9Hz), 1.25(3H,t,J = 7.1Hz), 1.29(3H,t,J = 7.1Hz), 2.57(3H,s), 2.68(2H,q,J = 7.4Hz), 2.78(1H,t,J = 7.1Hz), 3.44(1H,q,J = 7.1Hz), 3.58(1H,q,J = 7.1Hz), 3.70(1H,t,J = 7.4Hz), 3.79(1H,t,J = 7.4Hz), 4.10(1H,q,J = 7.1Hz), 4.18(1H,q,J = 7.1Hz), 5.21(1H,s), 5.23(1H,s), 6.43(1H,s), 7.48(1H,s), 7.5-7.9(3H,m), 2.84(1H,t,J = 7.1Hz)
	177	(solvent:CDCl ₃) 1.25(3H,t,J = 7.4Hz), 1.29(3H,d,J = 6.3Hz), 2.58(3H,s), 2.69(2H,q,J = 7.4Hz), 4.4-4.6(1H,m), 4.7-4.9(1H,m), 5.30(2H,s), 6.50(1H,s), 7.50(1H,s), 7.66(1H,d,J = 7.6Hz), 7.93(1H,dd,J = 7.6,7.6Hz), 8.13(1H,d,J = 7.6Hz)

Table 124

Ex. No.	Structural formula
1 7 8	

EP 0 516 069 A1

Table 125

	¹ H-NMR	δppm
5	178 (solvent:CDCl ₃) 1.23(1.2H,t,J = 7.6Hz), 1.26(1.8H,t,J = 7.6Hz), 2.1-2.6(2H,m), 2.59(3H,s), 2.8-3.0(2H,m), 3.8-4.8(3H,m), 5.3-5.4(3H,m), 6.44(0.6H,s), 6.48(0.4H,s), 7.5-8.1(3H,s)	
10		

15

20

25

30

35

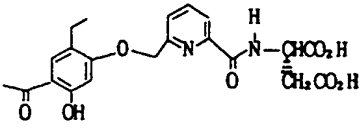
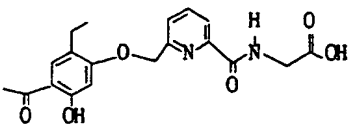
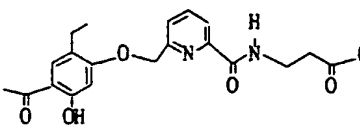
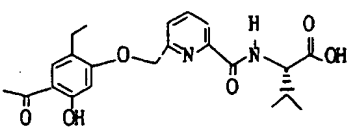
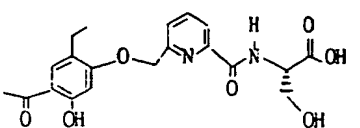
40

45

50

55

Table 126

	¹ H-NMR	δ ppm
1 7 9		
1 8 0		
1 8 1		
1 8 2		
1 8 3		

EP 0 516 069 A1

Table 127

		¹ H-NMR	δppm
5	179	(solvent: CD ₃ OD/CDCl ₃ (1/4)) 1.26(3H,t,J = 7.4Hz), 2.60(3H,s), 2.70(2H,q,J = 7.4Hz), 2.97(1H,dd,J = 17.5,4.8Hz), 3.15(1H,dd,J = 17.5,4.8Hz), 5.00(1H,t,J = 8.9Hz), 5.29(2H,s), 6.47(1H,s), 7.53(1H,s), 7.68(1H,d,J = 7.9Hz), 7.95(1H,dd,J = 7.9,7.6Hz), 8.11(1H,d,J = 7.6Hz)	
10	180	(solvent:d ₆ -DMSO) 1.18(3H,t,J = 7.6Hz), 2.58(3H,s), 2.62(2H,q,J = 7.6Hz), 4.00(2H,d,J = 5.9Hz), 5.36(2H,s), 6.57(1H,s), 7.69(1H,s), 7.73(1H,d,J = 6.3Hz), 8.01(1H,d,J = 6.3Hz), 8.10(1H,dd,J = 6.3Hz,6.3Hz), 8.88(1H,t,J = 5.9Hz), 12.55(1H,s)	
15	181	(solvent:d ₆ -DMSO) 1.18(3H,s,J = 7.6Hz), 2.58(3H,s), 2.61(2H,q,J = 7.6Hz), 2.69(2H,q,J = 7.6Hz), 3.4-3.5(2H,m), 5.35(2H,s), 6.57(1H,s) 7.69(1H,s), 7.70(1H,dd,J = 1.0Hz,7.6Hz), 7.99(1H,dd,J = 1.0Hz,7.6Hz), 8.07(1H,dd,J = 7.6Hz,7.6Hz), 8.72(1H,t,J = 5.9Hz), 12.54(1H,br)	
20	182	(solvent:d ₆ -DMSO) 0.91(6H,t,J = 6.4Hz), 1.18(3H,t,J = 7.6Hz), 2.1-2.2(1H,m), 2.57(3H,s), 2.63(1H,q,J = 7.6Hz), 4.41(1H,dd,J = 5.1Hz,8.9Hz), 5.42(2H,s), 6.63(1H,s), 7.68(1H,s), 7.76(1H,d,J = 6.6Hz), 8.01(1H,d,J = 6.9Hz), 8.11(1H,dd,J = 6.6Hz,6.9Hz), 8.38(1H,d,J = 8.9Hz), 12.55(1H,s)	
25	183	(solvent:d ₆ -DMSO) 1.19(3H,t,J = 7.6Hz), 2.58(3H,s), 2.63(2H,q,J = 7.6Hz), 3.77(1H,dd,J = 3.6Hz,10.9Hz), 3.91(1H,dd,J = 3.6Hz,10.9Hz), 4.4-4.5(1H,s) 5.39(2H,s) 6.61(1H,s), 7.69(1H,s), 7.75(1H,d,J = 7.6Hz), 8.03(1H,dd,J = 1.0Hz,7.6Hz), 8.11(1H,dd,J = 7.6Hz,7.6Hz), 8.63(1H,d,J = 8.3Hz), 12.55(1H,s)	

25

30

35

40

45

50

55

Table 128

Ex. No.	Structural formula
1 8 4	 <chem>CC(=O)c1ccc(O)cc1OCc2ccncc2C(=O)N[C@@H](C)C(=O)O</chem>
1 8 5	 <chem>c1ccccc1[C@@H](C(=O)O)N[C@@H](C(=O)c2ccncc2OCc3ccc(O)cc3OC)c4ccncc4</chem>
1 8 6	 <chem>Oc1ccc([C@@H](C(=O)O)N[C@@H](C(=O)c2ccncc2OCc3ccc(O)cc3OC)Cc4ccncc4)cc1</chem>
1 8 7	 <chem>C1=CN=C[C@H]1[C@@H](C(=O)O)N[C@@H](C(=O)c2ccncc2OCc3ccc(O)cc3OC)Cc4ccncc4</chem>
1 8 8	 <chem>CN1C=NC=C1[C@@H](C(=O)O)N[C@@H](C(=O)c2ccncc2OCc3ccc(O)cc3OC)Cc4ccncc4</chem>

EP 0 516 069 A1

Table 129

		¹ H-NMR	δppm
5	184	(solvent:d ₆ -DMSO) 1.18(3H,t,J = 7.6Hz), 2.04(3H,s), 2.1-2.2(2H,m), 2.4-2.5(2H,m), 2.58(3H,s), 2.62(2H,q,J = 7.6Hz), 4.5-4.6(1H,m), 5.40(2H,s), 6.60(1H,s), 7.69(1H,s), 7.74(1H,d,J = 7.6Hz), 7.99(1H,d,J = 6.6Hz), 8.09(1H,dd,J = 6.6Hz,7.6Hz), 8.74(1H,d,J = 8.2Hz), 12.55(1H,s)	
10	185	(solvent:d ₆ -DMSO) 1.16(3H,t,J = 7.6Hz), 2.59(3H,s), 2.63(2H,q,J = 7.6Hz), 3.1-3.4(2H,m), 4.6-4.7(1H,m), 5.34(2H,s), 6.60(1H,s), 7.1-7.3(5H,m), 7.68(1H,s), 7.71(1H,d,J = 7.6Hz), 7.97(1H,dd,J = 1.0Hz,7.6Hz), 8.07(1H,dd,J = 7.6Hz,7.6Hz), 8.61(1H,d,J = 8.2Hz), 12.56(1H,s)	
15	186	(solvent:d ₆ -DMSO) 1.17(3H,t,J = 7.6Hz), 2.58(3H,s), 2.61(2H,q,J = 7.6Hz), 3.5-3.6(2H,m), 4.6-4.7(1H,m), 5.36(1H,s), 6.62(2H,d,J = 8.5Hz),6.99(2H,d,J = 8.5Hz), 7.69(1H,s), 7.73(1H,dd,J = 1.0Hz,7.6Hz), 7.96(1H,dd,J = 1.0Hz),7.6Hz) 8.08(1H,dd,J = 7.6Hz,7.6Hz), 8.52(1H,d,J = 8.3Hz), 9.21(1H,br), 12.56(1H,s)	
20	187	(solvent:d ₆ -DMSO) 1.17(3H,t,J = 7.6Hz), 2.58(3H,s), 2.62(2H,q,J = 7.6Hz), 3.20(2H,d,J = 6.3Hz), 4.7-4.8(1H,m), 5.37(2H,s), 6.60(1H,s), 7.12(1H,s), 7.69(1H,s), 7.72(1H,d,J = 7.6Hz),7.98(1H,dd,J = 0.7Hz,7.6Hz) 8.08(1H,dd,J = 7.6Hz,7.6Hz), 8.28(1H,s) 8.99(1H,d,J = 8.3Hz), 12.54(1H,br),	
	188	(solvent:d ₆ -DMSO) 1.89(3H,t,J = 7.6Hz), 1.43(3H,d,J = 7.3Hz), 2.58(3H,s), 2.63(2H,q,J = 7.6Hz), 4.4-4.5(1H,m), 5.39(2H,s), 6.59(1H,s), 7.69(1H,s), 7.73(1H,d,J = 7.6Hz), 8.00(1H,d,J = 7.6Hz), 8.09(1H,dd,J = 7.6Hz,7.6Hz), 8.67(1H,d,J = 7.9Hz), 12.55(1H,s)	

25

30

35

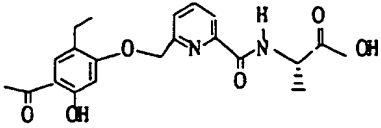
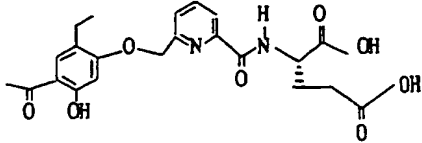
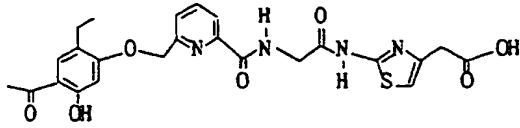
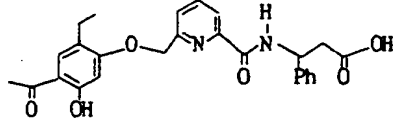
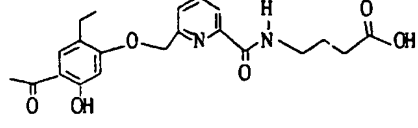
40

45

50

55

Table 130

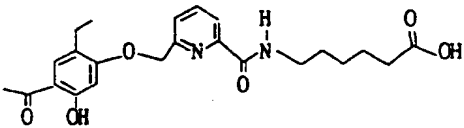
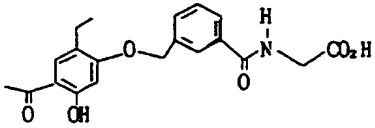
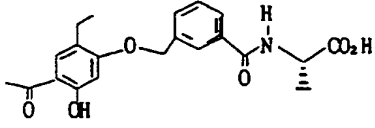
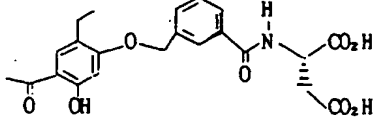
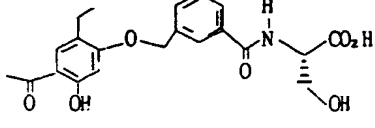
Ex. No.	Structural formula
189	
190	
191	
192	
193	

EP 0 516 069 A1

Table 131

	¹ H-NMR	δppm
5	189	(solvent:d ₆ -DMSO) 1.89(3H,t,J = 7.6Hz), 1.43(3H,d,J = 7.3Hz), 2.58(3H,s), 2.63(2H,q,J = 7.6Hz), 4.4-4.5(1H,m), 5.39(2H,s), 6.59(1H,s), 7.69(1H,s), 7.73(1H,d,J = 7.6Hz), 8.00(1H,d,J = 7.6Hz), 8.09(1H,dd,J = 7.6Hz,7.6Hz), 8.67(1H,d,J = 7.9Hz), 12.55(1H,s)
10	190	(solvent:d ₆ -DMSO) 1.86(3H,t,J = 7.6Hz), 1.9-2.3(4H,m), 2.58(3H,s), 2.63(2H,q,J = 7.6Hz), 4.4-4.5(1H,m), 5.40(2H,s), 6.60(1H,s), 7.69(1H,s), 7.73(1H,d,J = 7.6Hz), 8.00(1H,d,J = 7.6Hz), 8.10(1H,dd,J = 7.6Hz,7.6Hz), 8.70(1H,d,J = 8.6Hz), 12.55(1H,s)
15	191	(solvent:d ₆ -DMSO) 1.19(3H,t,J = 7.6Hz), 2.58(3H,s), 2.63(2H,q,J = 7.6Hz), 3.60(2H,s), 4.24(2H,d,J = 5.9Hz), 5.38(2H,s), 6.58(1H,s), 6.96(1H,s), 7.70(1H,s), 7.75(1H,d,J = 7.6Hz), 8.02(1H,d,J = 7.6Hz), 8.10(1H,dd,J = 7.6Hz,7.6Hz), 8.98(1H,d,J = 5.9Hz), 12.34(1H,br), 12.55(1H,s)
20	192	(solvent:d ₆ -DMSO) 1.17(3H,t,J = 7.6Hz), 2.58(3H,s), 2.62(2H,q,J = 7.6Hz), 2.88(1H,dd,J = 6.3Hz,16.2Hz), 4.0-4.2(1H,m), 5.39(2H,s), 5.4-5.5(1H,m), 6.60(1H,s), 7.2-7.7(5H,m), 7.69(1H,s), 7.72(1H,d,J = 7.6Hz), 7.98(1H,d,J = 7.3Hz), 8.07(1H,dd,J = 7.3Hz,7.6Hz), 9.13(1H,d,J = 8.9Hz), 12.32(1H,br), 12.56(1H,s)
25	193	(solvent:d ₆ -DMSO) 1.18(3H,t,J = 7.6Hz), 1.7-1.8(2H,m), 2.26(2H,t,J = 7.6Hz), 2.58(3H,s), 2.62(2H,q,J = 7.6Hz), 3.3-3.5(2H,m), 5.36(2H,s), 6.57(1H,s), 7.69(1H,s), 7.70(1H,d,J = 7.6Hz), 7.98(1H,d,J = 7.6Hz), 8.06(1H,dd,J = 7.6Hz,7.6Hz), 8.68(1H,d,J = 5.6Hz), 12.00(1H,br), 12.55(1H,br)

Table 132

Ex. No.	Structural formula
1 9 4	
1 9 5	
1 9 6	
1 9 7	
1 9 8	

EP 0 516 069 A1

Table 133

	¹ H-NMR	δppm
5	194	(solvent:DMSO-d ₆) 1.18(3H,t,J = 7.6Hz), 1.2-1.3(2H,m), 1.5-1.7(4H,m), 2.21(2H,t,J = 7.3Hz), 2.58(3H,s), 2.62(2H,q,J = 7.6Hz), 5.36(2H,s), 6.57(1H,s), 7.68(1H,d,J = 7.6Hz), 7.69(1H,s), 7.98(1H,d,J = 7.6Hz), 8.06(1H,dd,J = 7.6Hz,7.6Hz), 8.61(1H,m), 12.55(1H,br)
10	195	(solvent:CD ₃ OD/CDCl ₃ (1/4)) 1.21(3H,t,J = 7.6Hz), 2.58(3H,s), 2.64(2H,q,J = 7.6Hz), 4.18(2H,d,J = 1.7Hz), 5.16(2H,s), 6.46(1H,s), 7.49(1H,s), 7.50(1H,dd,J = 7.6,7.6Hz), 7.61(1H,d,J = 7.6Hz), 7.81(1H,d,J = 7.6Hz), 7.91(1H,s),
15	196	(solvent:CD ₃ OD:CDCl ₃ = 1:4) 1.22(3H,t,J = 7.4Hz), 1.55(3H,d,J = 6.9Hz), 2.58(3H,s), 2.64(2H,q,J = 7.4Hz), 4.72(1H,td,J = 5.9,7.3Hz), 5.17(2H,s), 6.46(1H,s), 7.50(1H,dd,J = 7.9,7.6Hz), 7.61(1H,d,J = 7.9Hz), 7.80(1H,d,J = 7.6Hz), 7.90(1H,s)
20	197	(solvent:CD ₃ OD:CDCl ₃ = 1:4) 1.22(3H,td,J = 7.6,0.9Hz), 2.65(2H,q,J = 7.6Hz), 2.98(1H,dd,J = 17.2,5.0Hz), 3.11(1H,dd,J = 17.5,5.0Hz), 4.99(1H,dt,J = 4.3,8.6Hz), 5.18(2H,s), 6.47(1H,s), 7.51(1H,dd,J = 7.6,8.3Hz), 7.63(1H,d,J = 8.3Hz), 7.81(1H,d,J = 7.6Hz), 7.92(1H,s), 2.59(3H,s), 7.51(1H,s)
25	198	(solvent:CD ₃ OD:CDCl ₃ = 1:4) 1.22(3H,t,J = 7.4Hz), 2.58(3H,s), 2.64(2H,q,J = 7.4Hz), 3.97(1H,dd,J = 11.6,3.5Hz), 4.10(1H,dd,J = 11.2,3.9Hz), 4.67(1H,t,J = 3.6Hz), 5.17(1H,s), 6.46(1H,s), 7.50(1H,s), 7.51(1H,dd,J = 7.6,7.6Hz), 7.62(1H,d,J = 7.6Hz), 7.85(1H,d,J = 7.6Hz)

25

30

35

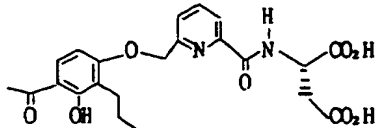
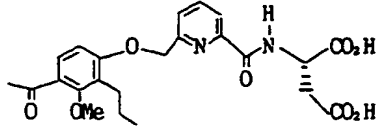
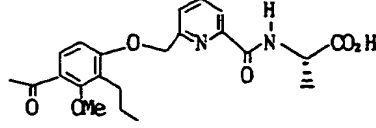
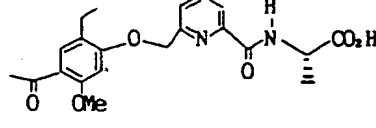
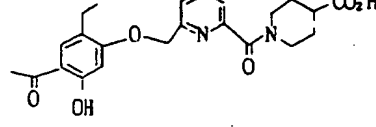
40

45

50

55

Table 134

Ex. No.	Structural formula
1 9 9	
2 0 0	
2 0 1	
2 0 2	
2 0 3	

EP 0 516 069 A1

Table 135

	¹ H-NMR	δppm
5	199	(solvent:CD ₃ OD/CDCl ₃ (1/4)) 0.99(3H,t,J = 7.6Hz), 1.5-1.7(2H,m), 2.60(3H,s), 2.70(2H,t,J = 7.8Hz), 3.0-3.3(2H,m), 5.1-5.2(1H,m), 5.27(2H,s) 6.76(2H,d,J = 8.9Hz), 7.53(2H,d,J = 8.9Hz), 7.64(1H,d,J = 7.9Hz), 7.90(1H,dd,J = 7.9,7.6Hz), 8.11(1H,d,J = 7.6Hz)
10	200	(solvent:CD ₃ OD/CDCl ₃ (1/4)) 0.98(3H,t,J = 7.3Hz), 1.5-1.7(2H,m), 2.57(3H,s), 2.75(2H,t,J = 7.6Hz), 3.0-3.3(2H,m), 3.75(3H,s), 5.1-5.2(1H,m), 5.31(2H,s), 6.50(1H,d,J = 8.9Hz), 7.60(1H,d,J = 8.9Hz), 7.67(1H,d,J = 7.6Hz), 7.92(1H,dd,J = 7.6,7.3Hz), 8.14(1H,d,J = 7.3Hz)
15	201	(solvent:CD ₃ OD/CDCl ₃ (1/4)) 1.01(3H,t,J = 7.3Hz), 1.63(3H,d,J = 7.3Hz), 1.5-1.7(2H,m), 2.62(3H,s), 2.74(2H,t,J = 7.6Hz), 3.78(3H,s), 4.80(1H,t,J = 7.3Hz), 5.29(2H,s), 6.73(1H,d,J = 8.9Hz), 7.55(1H,d,J = 8.9Hz), 7.66(1H,d,J = 7.6Hz), 7.93(1H,dd,J = 7.6,7.6Hz), 8.15(1H,d,J = 7.6Hz)
20	202	(solvent:CD ₃ OD/CDCl ₃ (1/4)) 1.23(3H,t,J = 7.4Hz), 1.62(3H,d,J = 7.3Hz), 2.58(3H,s), 2.69(2H,q,J = 7.4Hz), 3.87(3H,s), 4.82(1H,q,J = 7.3,7.3Hz), 5.31(2H,s), 6.49(1H,s), 7.71(1H,d,J = 7.9Hz), 7.71(1H,s), 7.94(1H,dd,J = 7.6,7.9Hz), 8.16(1H,d,J = 7.6Hz)
	203	(solvent: CD ₃ OD/CDCl ₃ (1/4)) 1.24(3H,t,J = 7.6Hz), 1.7-2.2(4H,m), 2.57(3H,s), 2.6-2.8(1H,m), 2.67(2H,q,J = 7.6Hz), 3.0-3.3(2H,m), 3.8-4.0(1H,m), 4.4-4.6(1H,m), 5.25(2H,s), 6.44(1H,s), 7.47(1H,s), 7.54(1H,d,J = 7.6Hz), 7.57(1H,d,J = 7.0Hz), 7.85(1H,dd,J = 7.6,7.9Hz)

25

30

35

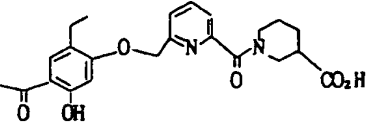
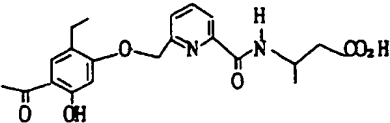
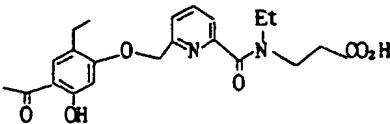
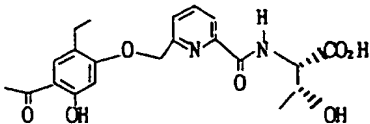
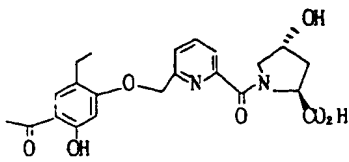
40

45

50

55

Table 136

Ex. No.	Structural formula
2 0 4	
2 0 5	
2 0 6	
2 0 7	
2 0 8	

EP 0 516 069 A1

Table 137

		¹ H-NMR	δppm
5	204	(solvent:CD ₃ OD/CDCl ₃ (1/4)) 1.25(3H,t,J = 7.4Hz), 1.5-2.3(5H,m), 2.57(3H,s), 2.67(2H,q,J = 7.4Hz), 2.7-2.9(1H,m), 3.1-4.8(4H,m), 5.25(2H,s), 6.44(1H,s), 7.47(1H,s), 7.5-7.7(2H,m), 7.85(1H,dd,J = 7.6,7.9Hz)	
10	205	(solvent: CD ₃ OD/CDCl ₃ (1/4)) 1.24(3H,t,J = 7.6Hz), 1.43(3H,d,J = 6.6Hz), 2.58(3H,s), 2.67(2H,q,J = 7.4Hz), 2.74(2H,dd,J = 5.6,3.0Hz), 4.5-4.6(1H,m), 5.25(2H,s), 6.51(1H,s), 7.48(1H,s), 7.61(1H,d,J = 7.9Hz), 7.89(1H,dd,J = 7.6,7.9Hz), 8.14(1H,d,J = 7.6Hz)	
	206	(solvent:CD ₃ OD/CDCl ₃ (1/4)) 1.2-1.3(6H,m), 2.57(1H,s), 2.67(2H,q,J = 7.5Hz), 2.8-3.0(2H,m), 3.4-3.8(4H,m), 5.24(2H,s), 6.4-6.5(1H,m), 7.48(1H,s), 7.5-7.7(2H,m), 7.85(1H,dd,J = 7.6,7.9Hz),	
15	207	(solvent:CD ₃ OD/CDCl ₃ (1/9)) 1.25(3H,t,J = 7.4Hz), 1.29(3H,d,J = 6.3Hz), 2.58(3H,s), 2.69(2H,q,J = 7.4Hz), 4.4-4.6(1H,m), 4.7-4.9(1H,m), 5.30(2H,s), 6.50(1H,s), 7.50(1H,s), 7.66(1H,d,J = 7.6Hz), 7.93(1H,dd,J = 7.6,7.6Hz), 8.13(1H,d,J = 7.6Hz)	
20	208	(solvent: CD ₃ OD/CDCl ₃ (1/9)) 1.23(1.2H,t,J = 7.6Hz), 1.26(1.8H,t,J = 7.6Hz), 2.1-2.6(2H,m), 2.59(3H,s), 2.8-3.0(2H,m), 3.8-4.8(3H,m), 5.3-5.4(3H,m), 6.44(0.6H,s), 6.48(0.4H,s), 7.5-8.1(3H,s),	

Table 138

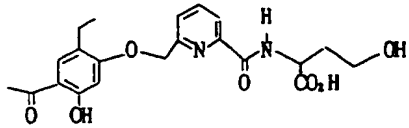
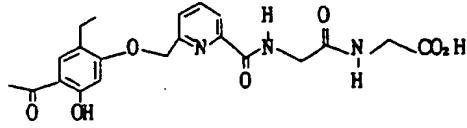
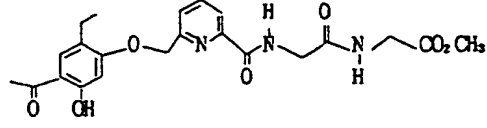
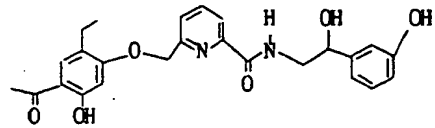
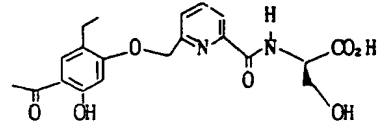
Ex. No.	Structural formula
2 0 9	
2 1 0	
2 1 1	
2 1 2	
2 1 3	

Table 139

	¹ H-NMR	δppm
209	(solvent:CDCl ₃ /MeOD(9/1)) 1.26(3H,t,J = 7.4Hz), 1.9-2.1(1H,m), 2.2-2.4(1H,m), 2.59(3H,s), 2.70(1H,q,J = 7.4Hz), 3.6-3.9(1H,m), 4.84(1H,dt,J = 4,3,4.6Hz), 5.30(2H,s), 6.49(1H,s), 7.53(1H,s), 7.69(1H,d,J = 7.6Hz), 7.96(1H,dd,J = 7.6,7.6Hz), 8.11(1H,d,J = 7.6Hz)	
210	(solvent:DMSO-d ₆) 1.19(3H,t,J = 7.6Hz), 2.57(3H,s), 2.63(2H,q,J = 7.6Hz), 3.78(2H,s), 4.02(2H,s), 5.36(2H,s), 6.56(1H,s), 7.67(1H,s), 7.71(1H,d,J = 7.3Hz), 8.03(1H,dd,J = 6.6,5.9Hz), 8.09(1H,d,J = 6.6Hz),	
211	(solvent:CDCl ₃ /MeOD(4/1)) 1.26(3H,t,J = 7.6Hz), 1.29(3H,t,J = 7.3Hz), 2.59(3H,s), 2.69(2H,q,J = 7.5Hz), 3.68(2H,s), 4.05(2H,s), 4.20(2H,q,J = 7.3Hz), 5.29(2H,s), 6.46(1H,s), 7.52(1H,s), 7.67(1H,d,J = 7.9Hz), 7.95(1H,dd,J = 7.6,7.9Hz), 8.11(1H,d,J = 7.6Hz)	
212	(solvent:DMSO-d ₆) 1.25(3H,t,J = 7.6Hz), 2.58(3H,s), 2.68(2H,q,J = 7.6Hz), 3.50(1H,m), 3.78(1H,m), 4.74(1H,m), 5.30(2H,s), 5.46(1H,d,J = 2.0Hz), 6.49(1H,s), 6.69(1H,m), 6.85(1H,d,J = 7.9Hz), 6.91(1H,s), 7.13(1H,t,J = 7.9Hz), 7.56(1H,s), 7.67(1H,d,J = 7.6Hz), 7.98(1H,t,J = 7.6Hz), 8.08(1H,d,J = 7.6Hz), 8.51(1H,m), 9.08(1H,s), 12.61(1H,s)	
213	(solvent:DMSO-d ₆) 1.19(3H,t,J = 7.6Hz), 2.58(3H,s), 2.64(2H,q,J = 7.6Hz), 3.85(2H,m), 4.55(1H,m), 5.34(1H,br), 5.39(2H,s), 6.60(1H,s), 7.68(1H,s), 7.74(1H,d,J = 7.6Hz), 8.05(1H,t,J = 7.6Hz), 8.12(1H,d,J = 7.6Hz), 8.63(1H,d,J = 8.3Hz), 12.55(1H,s), 12.90(1H,br)	

Table 140

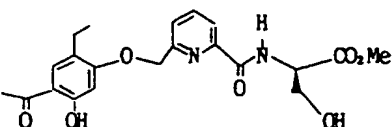
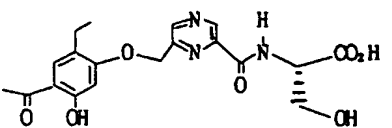
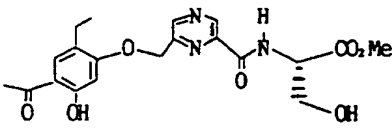
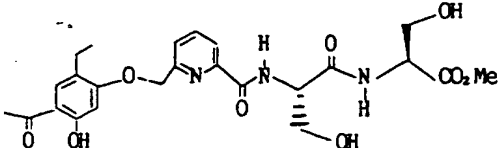
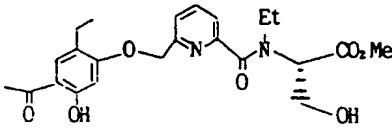
Ex. No.	Structural formula
2 1 4	
2 1 5	
2 1 6	
2 1 7	
2 1 8	

Table 141

	¹ H-NMR	δppm
5	214	(solvent:CDCl ₃) 1.25(3H,t,J = 7.6Hz), 2.58(3H,s), 2.68(2H,q,J = 7.6Hz), 3.85(3H,s), 4.11(2H,m), 4.88(1H,m), 5.29(2H,s), 6.52(1H,s), 7.49(1H,s), 7.65(1H,d,J = 8.3Hz), 7.91(1H,t,J = 8.3Hz), 8.15(1H,d,J = 8.3Hz), 8.80(1H,d,J = 8.3Hz) 12.69(1H,s)
10	215	(solvent:DMSO-d ₆) 1.18(3H,t,J = 7.3Hz), 2.51(3H,s), 2.63(2H,q,J = 7.3Hz), 3.79(1H,dd,J = 11.2Hz,3.9Hz), 3.91(1H,dd,J = 11.2Hz,3.9Hz), 4.55(1H,m), 5.48(2H,s), 6.68(1H,s), 7.70(1H,s), 8.58(1H,d,J = 7.9Hz), 9.05(1H,s), 9.21(1H,s), 12.57(1H,s)
15	216	(solvent:CDCl ₃) 1.27(3H,t,J = 7.3Hz), 2.59(3H,br), 2.89(3H,s), 2.68(2H,q,J = 7.3Hz), 3.85(3H,s), 4.06(1H,dd,J = 11.2Hz,3.6Hz), 4.18(1H,dd,J = 11.2Hz,3.6Hz), 4.90(1H,m), 5.34(2H,s), 6.52(1H,s), 7.51(1H,s), 8.58(1H,m), 9.00(1H,s), 9.37(1H,s), 12.71(1H,s),
20	217	(solvent:CDCl ₃) 1.27(3H,t,J = 7.6Hz), 2.60(3H,s), 2.71(2H,q,J = 7.6Hz), 3.79(2H,s), 3.85-4.10(4H,m), 4.64-4.80(2H,m), 5.33(2H,s), 6.49(1H,s), 7.57(1H,s), 7.72(1H,d,J = 7.6Hz), 8.00(1H,t,J = 7.6Hz), 8.10(1H,d,J = 7.6Hz)
	218	(solvent:CDCl ₃) 1.25(3H,t,J = 7.6Hz), 2.57(3H,s), 2.67(2H,q,J = 7.6Hz), 3.2-3.7(2H,m), 3.70(s,1.2H), 3.81(s,1.8H), 4.0-4.3(2H,m), 4.37(0.6H,m), 4.90(0.4H,m), 5.24(2H,s), 6.44(1H,s), 7.48(1H,s), 7.5-7.9(3H,m), 12.63(1H,s)

25

30

35

40

45

50

55

Ex. No.	Structural formula
2 1 9	
2 2 0	
2 2 1	
2 2 2	
2 2 3	

EP 0 516 069 A1

Table 143

	¹ H-NMR	δppm
5	219	(solvent:CDCl ₃) 1.00(3H,t,J = 7.6Hz), 1.24(3H,t,J = 7.6Hz), 1.81(2H,q,J = 7.6Hz), 2.58(3H,s), 2.67(2H,q,J = 7.6Hz), 3.72(2H,m), 3.94-4.06(4H,m), 5.27(2H,s), 6.56(1H,s), 7.48(1H,s), 7.63(1H,d,J = 7.6Hz), 7.93(1H,t,J = 7.6Hz), 8.15(1H,d,J = 7.6Hz), 8.52(1H,brs), 12.73(1H,s),
10	220	(solvent:CDCl ₃) 1.24(3H,t,J = 7.3Hz), 1.38(3H,s), 2.58(3H,s), 2.67(2H,q,J = 7.3Hz), 3.7-4.1(6H,m), 5.27(2H,s), 6.56(1H,s), 7.48(1H,s), 7.64(1H,d,J = 7.6Hz), 7.92(1H,t,J = 7.6Hz), 8.14(1H,d,J = 7.6Hz), 8.49(1H,s), 12.73(1H,s)
15	221	(solvent:CDCl ₃) 1.22(3H,t,J = 7.6Hz), 2.57(3H,s), 2.65(2H,q,J = 7.6Hz), 3.83(8H,s), 5.29(2H,s), 6.66(1H,s), 7.46(1H,s), 7.65(1H,d,J = 6.6Hz), 7.93(1H,t,J = 7.6Hz), 8.14(1H,d,J = 7.9Hz), 9.12(1H,s), 12.82(1H,s)
20	222	(solvent:CDCl ₃) 1.26(3H,t,J = 7.6Hz), 2.58(3H,s), 2.67-2.72(2H,m), 3.75-3.82(2H,m), 3.83-3.95(2H,m), 4.14-4.20(1H,m), 4.20-4.26(2H,m), 5.27(2H,s), 6.45(1H,s), 7.50(1H,s), 7.62(1H,d,J = 6.9Hz), 7.92(1H,t,J = 6.9Hz), 8.13(1H,d,J = 6.9Hz), 8.53(1H,d,J = 7.9Hz), 12.66(1H,s)
	223	(solvent:DMSO-d ₆) 1.21(3H,t,J = 7.6Hz), 2.58(3H,s), 2.65(2H,q,J = 7.6Hz), 3.7-3.9(4H,m), 4.61(1H,m), 5.05(1H,br), 5.37(2H,s), 6.58(1H,s), 7.65(1H,s), 7.71(1H,dd,J = 6.8Hz,2.1Hz), 8.02-8.25(2H,m), 8.39(1H,t,J = 5.8Hz), 8.62(1H,d,J = 8.3Hz), 12.54(1H,s),

25

30

35

40

45

50

55

Table 144

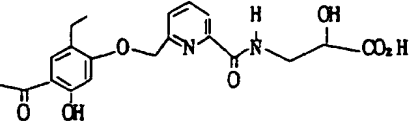
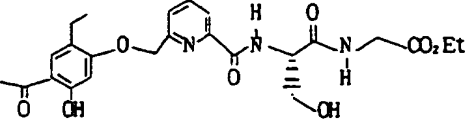
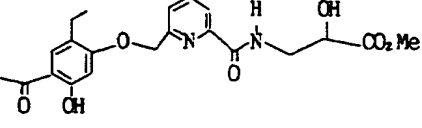
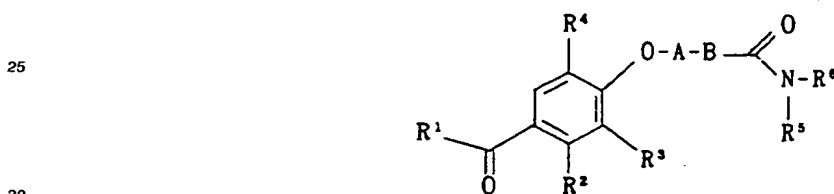
Ex. No.	Structural formula
2 2 4	
2 2 5	
2 2 6	

Table 145

	¹ H-NMR	δppm
5	224	(solvent:DMSO-d ₆) 1.21(3H,t,J = 7.6Hz), 2.57(3H,s), 2.64(2H,q,J = 7.6Hz), 3.54(1H,m), 3.72(1H,m), 4.19(1H,m), 5.34(2H,s), 5.59(1H,br), 6.55(1H,s), 7.63(1H,s), 7.69(1H,dd,J = 6.1Hz,2.8Hz), 8.05(2H,m), 8.51(1H,t,J = 6.1Hz), 12.55(1H,s), 12.65(1H,br)
10	225	(solvent:CDCl ₃) 1.25(3H,t,J = 7.6Hz), 1.26(3H,t,J = 7.3Hz), 2.58(3H,s), 2.68(2H,q,J = 7.6Hz), 3.10(1H,dd,J = 8.9Hz,5.6Hz), 3.80-3.88(1H,m), 4.06(2H,d,J = 5.6Hz), 4.20(2H,q,J = 7.3Hz), 4.25-4.35(1H,m), 4.70(1H,m), 5.28(2H,s), 6.45(1H,s), 7.15(1H,br), 7.49(1H,s), 7.63(1H,d,J = 6.9Hz), 7.92(1H,t,J = 6.9Hz), 8.15(1H,d,J = 6.9Hz), 8.85(1H,d,J = 7.6Hz), 12.66(1H,s)
15	226	(solvent:CDCl ₃) 1.25(3H,t,J = 7.6Hz), 2.58(3H,s), 2.68(2H,q,J = 7.6Hz), 3.57(1H,d,J = 5.3Hz), 3.83(3H,s), 3.88(2H,m), 4.44(1H,m), 5.25(2H,s), 6.47(1H,s), 7.49(1H,s), 7.63(1H,d,J = 7.6Hz), 7.91(1H,t,J = 7.6Hz), 8.14(1H,d,J = 7.6Hz), 8.36(1H,br), 12.68(1H,s)

Claims

- 20 1. A compound represented by the formula :



wherein

- A is a C₁-C₅ alkylene chain;
- 35 B is a phenylene or 6 membered heteroaromatic group which is constituted by carbon atoms and one or two nitrogen atoms, and B may be, optionally substituted with one or two substituents selected from the group, consisting of a C₁-C₅ alkyl group, a C₁-C₅ alkoxy group, a hydroxyl group, a carboxyl group, a nitro group and a halogen atom;
- R¹ is a C₁-C₅ alkyl group;
- 40 R² is a hydroxyl group or a C₁-C₅ alkoxy group;
- R³ and R⁴ are each independently a hydrogen atom, a C₁-C₅ alkyl group, a C₂-C₅ alkenyl group or a C₂-C₅ alkynyl group;
- R⁵ is a hydrogen atom, a C₁-C₅ alkyl group or a hydroxy C₁-C₅ alkyl group;
- R⁶ is a group of the formula:

45 -X-Y-Z-R^{6'}

wherein X is a phenylene group or a monocyclic 5- 6 membered hetero aromatic group, and X is optionally substituted with one or two substituents selected from the group consisting of a C₁-C₅ alkyl group, a hydroxyl group, a carboxyl group, a nitro group and a halogen atom;

- 50 Y is a single bond or an oxygen atom;
- Z is a single bond or a C₁-C₅ alkylene chain;
- provided that when Y is an oxygen atom,
- X is a phenylene group and Z is a C₁-C₅ alkylene chain;
- 55 R^{6'} is a COOR⁷ group,
- a CONR⁸R⁹ group,
- a CONHCHR²⁰(CH₂)_nCOOR⁷ group,
- a CONHCHR²⁰(CH₂)_nCONR⁸R⁹ group,
- a CONHCHR²⁰CONHCHR²²CO₂R⁷ group or

a sulfamoyl group,
wherein R⁷ is a hydrogen atom, a benzyl group, a C₁-C₅ alkyl group or an C₁-C₅ alkyl group substituted with an aminoheteroaromatic group wherein the heteroaromatic group is a monocyclic 5-6 membered heteroaromatic group;

5 R⁸ and R⁹ are each independently a hydrogen atom, a C₁-C₅ alkyl group, hydroxy C₁-C₅ alkyl group, a hydroxyethylpyridyl group or a hydroxyethylthiazolyl group, or the group of the formula:



10 represents a pyrrolidino, a piperidino or a morpholino group;

R²⁰ is a hydrogen atom, a hydroxyl group, a C₁-C₅ alkyl group, a phenyl group, a hydroxyphenyl group, a benzyl group, a hydroxy benzyl group or a substituted C₁-C₅ alkyl group wherein the substituent is selected from the group consisting of a hydroxyl group, a C₁-C₅ alkoxy group, a mercapto group, a methylthio group, an amino group, an indolyl group, an imidazolyl group, a carboxyl group, a C₁-C₅ alkoxycarbonyl group, a carbamoyl group and a guanidino group;

n is 0, 1, 2, 3, 4 or 5; and

R²² is a hydrogen atom, a C₁-C₅ alkyl group or a C₁-C₅ hydroxyalkyl group;

or R⁶ is a CHR²⁰(CH₂)_nCOOR⁷ group,

a CH₂CHR²⁰COOR⁷ group,

20 a CHR²⁰(CH₂)_nCONR⁸R⁹ group,

a CH₂CHR²⁰CONR⁸R⁹ group,

a CHR²⁰(CH₂)_nOH group,

a CR²⁰R²²(CH₂)_nOH group,

a CH₂CHR²⁰OH group, or

25 a CHR²⁰CONHCHR²²CO₂R⁷ group,

wherein R⁷, R⁸, R⁹, R²⁰, R²² and n are as defined above, or the group of the formula:



35 represents an azetidino group, pyrrolidino group, a piperidino group or a homopiperidino group, which is optionally substituted with one to two substituents selected from the group consisting of a hydroxyl group, a C₁-C₅ hydroxyalkyl group, carboxyl group, C₁-C₅ alkoxycarbonyl group and benzyloxycarbonyl group; or pharmaceutically acceptable salts thereof.

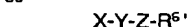
40 2. The compound according to claim 1, wherein R¹ is a methyl group and R² is a hydroxyl group.

3. The compound according to claim 1, wherein R³ is a hydrogen atom and A is a methylene group.

4. The compound according to claim 1, wherein R¹ is a methyl group, R² is a hydroxyl group, R³ is a hydrogen atom and A is a methylene group.

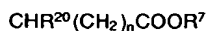
45 5. The compound according to claim 4, wherein B is a 2,6-pyridinediyl, a 2,4-pyrimidinediyl or a 2,6-pyridinediyl N-oxide group.

6. The compound according to claim 4, wherein R⁶ is a group of the formula:



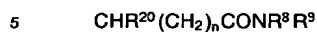
(wherein X, Y, Z and R^{6'} are as defined in claim 1).

55 7. The compound according to claim 4, wherein R⁶ is a group of the formula:



(wherein R^{20} , R^7 and n are as defined in claim 1).

8. The compound according to claim 4, wherein R^6 is a group of the formula:



(wherein R^{20} , R^8 , R^9 and n are as defined in claim 1).

9. The compound according to claim 4, wherein R^6 is a group of the formula:

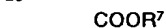


(wherein R^{20} , R^{22} , R^7 and n are as defined in claim 1).

15 10. The compound according to claim 4, wherein R^4 is an ethyl group.

11. The compound according to claim 5, wherein X is a 2,6-pyridinediyl group.

12. The compound according to claim 10, wherein $R^{6'}$ is a group of the formula:



(wherein R^7 is as defined in claim 1).

25 13. The compound according to claim 13, wherein $R^{6'}$ is a carboxyl group.

14. The compound according to claim 10, wherein $R^{6'}$ is a group of the formula:

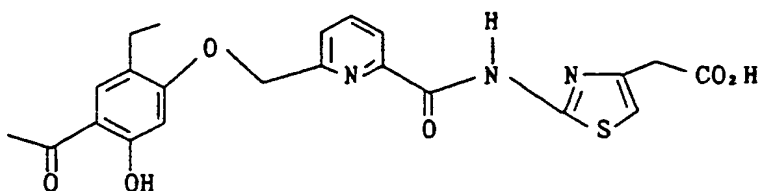


(wherein R^{20} , R^7 and n are as defined in claim 1).

15. A compound of the formula:

35

40

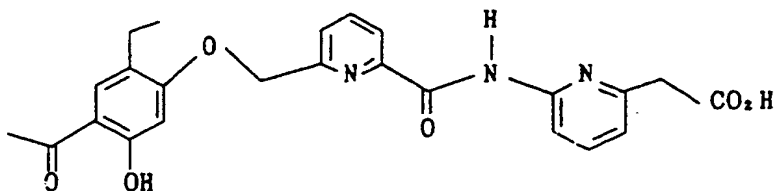


45

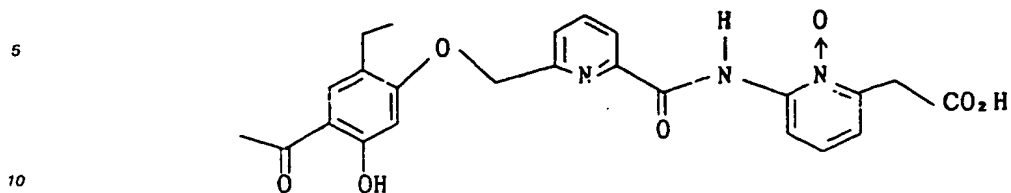
16. A compound of the formula:

50

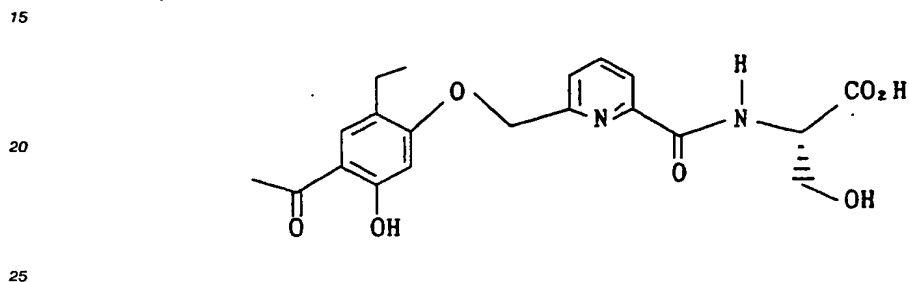
55



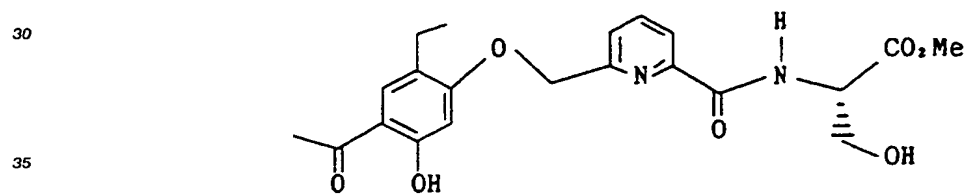
17. A compound of the formula:



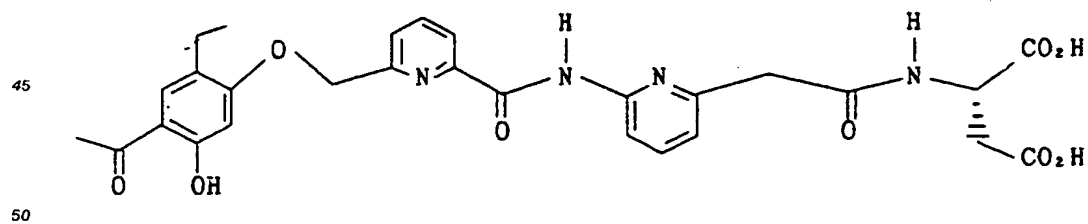
18. A compound of the formula:



19. A compound of the formula:



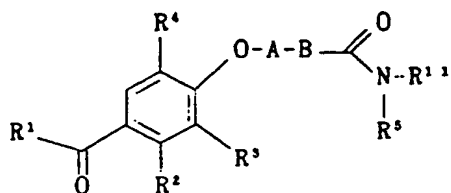
40 20. A compound of the formula:



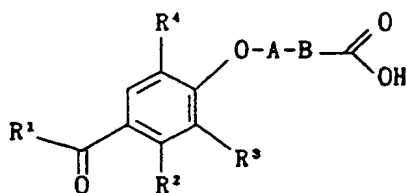
21. A process for producing a compound as claimed in claim 1 which comprises:

(a) to produce a compound of the formula:

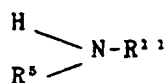
55



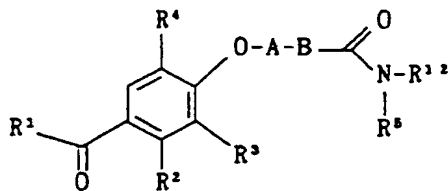
reacting a compound of the formula:



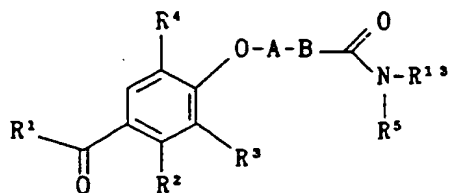
with a compound of the formula:



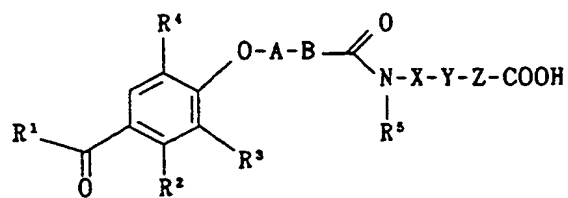
(b) hydrolyzing a compound of the formula:



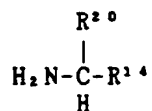
to produce a compound of the formula:



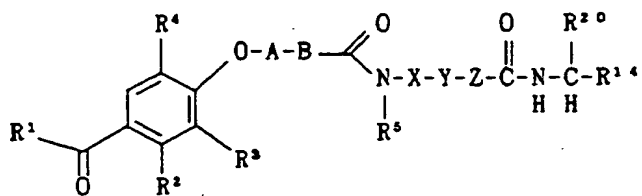
(c) reacting a compound of the formula:



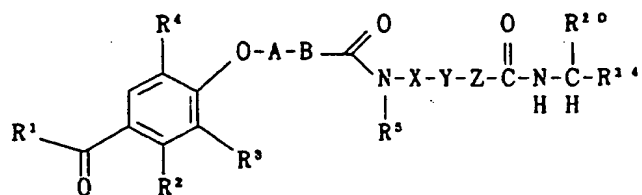
with a compound of the formula:



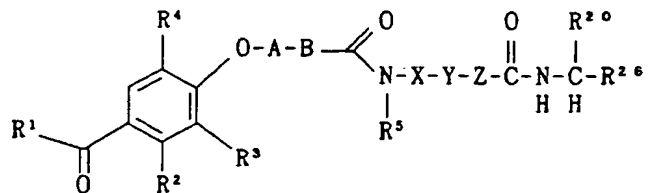
to produce a compound of the formula:



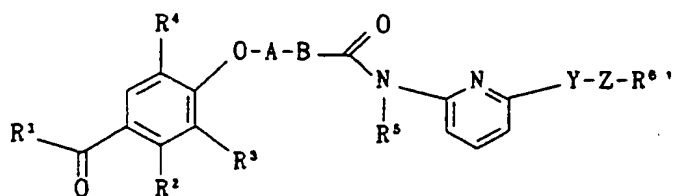
(d) hydrolyzing a compound of the formula:



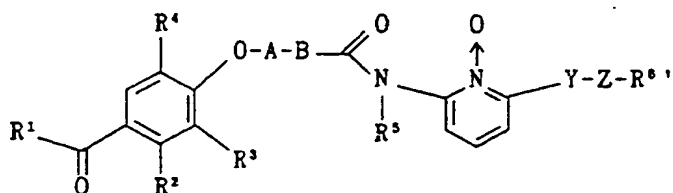
to produce a compound of the formula:



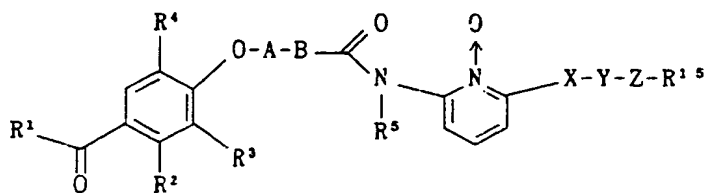
(e) oxidizing a compound of the formula:



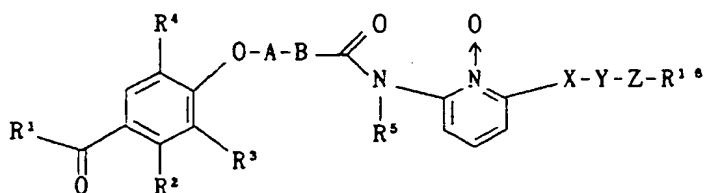
to produce a compound of the formula:



or
(f) hydrolyzing a compound of the formula.



to produce a compound of the formula:



wherein R^1 , R^2 , R^3 , R^4 , R^5 , $R^{6'}$, R^{20} , A , B , X , Y and Z are as defined in claim 1,

R^{11} is the same as $R^{6'}$, but it does not mean free carboxylic group;

R^{12} is a group of the formula:

$X-Y-Z-COOR^{7'}$,
 $X-Y-Z-CONHCHR^{20}(CH_2)_n COOR^{7'}$,
 $X-Y-Z-CONHCHR^{20}CONHCHR^{22}CO_2R^{7'}$,
 $CHR^{20}(CH_2)_n COOR^{7'}$,
 $CH_2 CHR^{20} COOR^{7'}$, or
 $CHR^{20} CONHCHR^{22} COOR^{7'}$,

wherein X, Y, Z, R²⁰, R²² and n are as defined above, and R^{7'} is the same as R⁷ but it does not mean a hydrogen atom,

R¹³ is a group of the formula:

5 X-Y-Z-COOH,
X-Y-Z-CONHCHR²⁰(CH₂)_nCOOH,
X-Y-Z-CONHCHR²⁰CONHCHR²²CO₂H,
CHR²⁰(CH₂)_nCOOH,
CH₂CHR²⁰COOH, or
10 CHR²⁰CONHCHR²²COOH,

wherein X, Y, Z, R²⁰, R²² and n are as defined above.

R¹⁴ is a group of the formula:

15 (CH₂)_nCOOR^{7'}, or
CONHCHR²²COOR^{7'},

wherein R^{7'}, R²² and n are as defined above.

R¹⁵ is a group of the formula:

20 COOR^{7'},
CONHCHR²⁰(CH₂)_nCOOR^{7'}, or
CONHCHR²⁰CONHCHR²²CO₂R^{7'},

25 wherein R^{7'}, R²⁰, R²² and n are as defined above.

R¹⁶ is a group of the formula:

30 COOH,
CONHCHR²⁰(CH₂)_nCOOH, or
CONHCHR²⁰CONHCHR²²CO₂H,

wherein R²⁰, R²² and n are as defined above.

R²⁶ is a group of the formula:

35 (CH₂)_nCOOH, or
CONHCHR²²COOH,

wherein R²² and n are as defined above.

40 22. A pharmaceutical composition useful as an antiinflammatory agent or an antiallergic agent, which comprises an effective amount of a compound of claim 1 or a pharmaceutically acceptable salt thereof as an active ingredient and a pharmaceutically acceptable carrier or diluent.

45 23. A method of treating inflammatory or allergic states which comprises administering a pharmaceutically effective amount of a compound of claim 1 or a pharmaceutically acceptable salt thereof to a patient.

24. A compound of claim 1 for use as a medicament as an active therapeutic substance.

50

55



European Patent
Office

PARTIAL EUROPEAN SEARCH REPORT

which under Rule 45 of the European Patent Convention
shall be considered, for the purposes of subsequent
proceedings, as the European search report

Application Number

EP 92 10 8916

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl. 5)
Y	US-A-4 672 066 (M. CARSON et al.) * Claims 1-4,6,15,16,30; examples 31-38 * ---	1-5,22, 24	C 07 D 213/81 C 07 D 277/46 C 07 D 401/06 C 07 D 401/12 C 07 D 401/14 C 07 D 417/12 C 07 D 417/14 C 07 D 241/24 C 07 C 233/82 A 61 K 31/44 A 61 K 31/425
Y	CHEMICAL ABSTRACTS, vol. 111, no. 11, 11th September 1989, page 729, abstract no. 97094e, Columbus, Ohio, US; & JP-A-01 29 363 (YOSHITOMI PHARMACEUTICAL INDUSTRIES, LTD) 31-01-1989 * Abstract * ---	1-5,22, 24	
X	* CAS RN 122151-73-9 * ---	1-5,22, 24	
A	CHEMICAL ABSTRACTS, vol. 112, no. 3, 15th January 1990, page 494, abstract no. 20906j, Columbus, Ohio, US; & JP-A-01 104 052 (YOSHITOMI PHARMACEUTICAL INDUSTRIES, LTD) 21-04-1989 * Abstract * --- -/-	1-22,24	
			TECHNICAL FIELDS SEARCHED (Int. Cl. 5)
			C 07 D C 07 C A 61 K
INCOMPLETE SEARCH			
<p>The Search Division considers that the present European patent application does not comply with the provisions of the European Patent Convention to such an extent that it is not possible to carry out a meaningful search into the state of the art on the basis of some of the claims</p> <p>Claims searched completely : Claims searched incompletely : Claims not searched : Reason for the limitation of the search:</p> <p>Remark: Although claim 23 is directed to a method of treatment of (diagnostic method practised on) the human/animal body (Art. 52(4) EPC) the search has been carried out and based on the alleged effects of the compound/composition.</p>			
Place of search THE HAGUE		Date of completion of the search 01-09-1992	Examiner BOSMA P.
CATEGORY OF CITED DOCUMENTS			
X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document			
T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons ----- & : member of the same patent family, corresponding document			



European Patent
Office

PARTIAL EUROPEAN SEARCH REPORT

Application Number

EP 92 10 8916

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int. Cl. 5)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
A,D	EP-A-0 276 065 (ELI LILLY AND CO.) * Claims 1-7; examples * ---	1-20,22 ,24	
A	EP-A-0 174 770 (MERCK FROSST CANADA INC.) * Whole document * -----	1-22,24	
			TECHNICAL FIELDS SEARCHED (Int. Cl.5)



Eur päisches Patentamt
European Patent Office
Office européen des brevets



Publication number: **0 516 069 A1**

(12)

EUROPEAN PATENT APPLICATION

(21) Application number: **92108916.5**

(22) Date of filing: **27.05.92**

(51) Int. Cl.⁵: **C07D 213/81, C07D 277/46, C07D 401/06, C07D 401/12, C07D 401/14, C07D 417/12, C07D 417/14, C07D 241/24, C07C 233/82, A61K 31/44, A61K 31/425**

(30) Priority: **31.05.91 JP 157725/91**

(43) Date of publication of application:
02.12.92 Bulletin 92/49

(94) Designated Contracting States:
AT BE CH DE DK ES FR GB GR IT LI NL PT SE

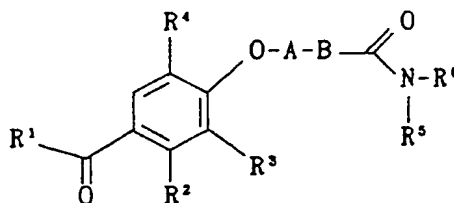
(71) Applicant: **SUMITOMO PHARMACEUTICALS COMPANY, LIMITED**
2-8, Doshomachi 2-chome, Chuo-ku
Osaka-shi Osaka 541(JP)

(72) Inventor: **Nagata, Hideo**
2-29-7, Ooike
Ibaraki-shi, Osaka 567(JP)
Inventor: **Kawakami, Hajime**
6-32-702, Fukazu-cho
Nishinomiyashi, Hyogo 663(JP)

(74) Representative: **von Kreisler, Alek,**
Dipl.-Chem. et al
Patentanwälte Von Kreisler-Selting-Werner,
Deichmannhaus am Hauptbahnhof
W-5000 Köln 1(DE)

(54) **Leukotriene B₄ antagonist.**

(57) Leukotriene B₄ antagonists of the formula:



wherein each symbol is as defined in the specification, processes for producing them, and pharmaceutical compositions containing them. The compounds of the present invention are very useful as the drugs for the treatment of allergic and inflammatory diseases.

EP 0 516 069 A1

pfs no=91157725 cc=JP ls

NO : 91 157725 CC : JP

FAMILY MEMBERS

CC	PUBDAT	KD	DOC.NO.	CC	PR.DAT	YY	PR.NO.
					JP 1991/05/31	91	157725

AT 1996/05/15 E 137223

AU 1993/03/11 A1 1719392

AU 1993/11/04 B2 643140

CA 1992/12/01 AA 2069667

DE 1996/05/30 C0 69210091

DE 1996/10/02 T2 69210091

DK 1996/05/13 T3 516069

EP 1992/12/02 A1 516069

DC : AT BE CH DE DK ES FR GB GR IT LI NL PT SE

EP 1996/04/24 B1 516069

DC : AT BE CH DE DK ES FR GB GR IT LI NL PT SE

ES 1996/07/01 T3 2086579

GR 1996/08/31 T3 3020050

JP 1993/09/17 A2 5239004

MX 1993/01/20 A1 9202612

US 1993/07/06 A 5225422